In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

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CATHERINE GERTRUDE McCABE,	*	
	*	No. 13-570V
Petitioner,	*	Special Master Christian J. Moran
	*	
v.	*	Filed: May 17, 2018
	*	
SECRETARY OF HEALTH	*	Entitlement, flu vaccine,
AND HUMAN SERVICES,	*	chronic fatigue syndrome.
	*	
Respondent.	*	
* *		

Clifford Shoemaker, Shoemaker, Gentry & Knickelbein, for petitioner;
Glenn MacLeod, United States Dep't of Justice, Washington, DC, for respondent.

PUBLISHED DECISION DENYING COMPENSATION[1]

Petitioner, Catherine Gertrude McCabe, alleges that influenza ("flu") vaccinations caused her to develop chronic fatigue syndrome ("CFS").[2] Ms. McCabe is seeking compensation pursuant to the National Childhood Vaccine Injury Compensation Program, codified at 42 U.S.C. § 300aa−10 through 34 (2012).

Ms. McCabe puts forth the opinions of two experts, who together argue that her 2010 flu vaccine, perhaps in conjunction with previous flu vaccines, caused dysregulation of Ms. McCabe's immune system and/or neurological damage. This

[1] The E-Government Act, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services), requires that the Court post this decision on its website. Pursuant to Vaccine Rule 18(b), the parties have 14 days to file a motion proposing redaction of medical information or other information described in 42 U.S.C. § 300aa-12(d)(4). Any redactions ordered by the special master will appear in the document posted on the website.

[2] There is a substantial amount of debate about the naming of the condition widely referred to as chronic fatigue syndrome. The syndrome has also been called myalgic encephalomyelitis ("ME") and a combination of the two: ME/CFS. The undersigned does not take any position on the name and uses CFS in this document. However, when referencing another source, the terminology used by the referenced source is used.

dysregulation and/or neurological damage, in turn, allegedly caused her to develop CFS, or significantly aggravated her pre-existing CFS. The Secretary disagrees. The Secretary argues that Ms. McCabe does not have CFS, that the flu vaccine cannot cause CFS, and even if it could, it did not do so here.

Ms. McCabe's claim fails for several overlapping reasons. The foundational issue is that Ms. McCabe's health before and after the 2010 flu vaccination appears unchanged. Without a persuasive showing that Ms. McCabe's health worsened, Ms. McCabe cannot establish that the September 11, 2010 flu vaccination either caused her to suffer from CFS or significantly aggravated her pre-existing CFS. In addition, the evidence does not support a diagnosis of CFS, a condition that none of Ms. McCabe's treating doctors have diagnosed her with. Furthermore, Ms. McCabe fails to present persuasive evidence supporting a potential causal link between the flu vaccine and CFS. As a result of petitioner's failure to demonstrate that she suffered a cognizable injury and her failure to provide sufficient evidence of causation, her claim for compensation must fail.

I. Facts

Information about the events in Ms. McCabe's life is drawn from two sources: records and testimony. The records primarily consist of medical records that describe her health. Because of the importance of contemporaneously created medical records (see Cucuras v. Sec'y of Health & Human Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993)), the medical records are summarized first, in section A below. Section B provides a summary of the oral testimony from Ms. McCabe.

A. Medical Records[3]

A critical issue is whether Ms. McCabe's health changed shortly after the September 11, 2010 flu vaccination. To facilitate an analysis that compares and contrasts her health, this section is divided into discrete times. Section 1 presents information from Ms. McCabe's medical records before September 11, 2010. Section 2 reviews Ms. McCabe's health for the year after the September 11, 2010 vaccination. Section 3 summarizes Ms. McCabe's health from 2011 until the most recent medical records were filed.

[3] Ms. McCabe also filed employment records, which are discussed in the context of comparing her functioning before and after vaccination. See Section IV.B.1, below.

1. Prior to the September 11, 2010 Flu Vaccination

Ms. McCabe was born on November 17, 1959. Ms. McCabe's primary care physician leading up to the time of her vaccination and for several years after was Dr. Ja Gu Kang. Unfortunately, portions of Dr. Kang's records are illegible. Though the entire record has been reviewed, the facts presented here focus on those portions of the record that legibly state Ms. McCabe's symptoms at her regular visits as well as other major health events (e.g., hospital visits). Because Ms. McCabe alleges the vaccine affected her chronic fatigue syndrome, specific emphasis is placed on records associated with fatigue (e.g., insomnia, depression, and records of treatment associated with fatigue).

In the years before her 2010 vaccination, Ms. McCabe repeatedly noted she experienced depression, insomnia, and/or fatigue. These features are noted on the following 20 dates: 10/2/06, 12/2/06, 1/6/07, 2/26/07, 3/9/07, 3/31/07, 5/12/07, 6/9/07, 9/29/07, 11/24/07, 5/12/08, 2/17/09, 5/2/09, 9/17/09, 10/19/09, 12/21/09, 2/19/10, 6/3/10, 7/15/10, and 9/11/10 (the date of the vaccination in question). Exhibit 1 at 1-12.[4]

Consistent with these reports of fatigue, Ms. McCabe also was repeatedly administered shots of vitamin B12. These shots are noted on 10/2/06, 3/9/07, 3/31/07, 4/7/07, 5/12/07, 6/9/07, 9/29/07, 11/10/07, 11/24/07, 5/12/08, 12/13/08, 2/19/10, 4/9/2010, and 7/15/2010 (14 times). The purpose of the B12 shots is not indicated in Dr. Kang's notes, but Ms. McCabe testified they were to help with her fatigue. See Tr. at 64 ("Lack of sleep and tiredness. I had been very tired. Now, I don't know if that's been ten years ago or if it's from the flu vaccine, but I am just constantly tired. So that's why I was getting B12 shots, to give me energy.") Ms. McCabe was also being treated with Effexor (an anti-depressant), Ambien (a sleep aid), and lorazepam (a benzodiazepine used to treat anxiety disorders, among other things). Exhibit 1 at 1-12.

In addition to fatigue, depression, and insomnia, Ms. McCabe's medical records indicate that she often presented with a persistent cough and diagnoses of COPD, bronchitis, and asthma were noted throughout Dr. Kang's record. Id.

Beyond these chronic conditions, Ms. McCabe's records indicate that she was treated for other injuries and diseases as well. On April 4, 2008, she was seen in emergency care for a fall. Exhibit 1 at 48; exhibit 3 at 88. X-rays showed no

[4] Due to the illegibility of Dr. Kang's handwriting, it is impossible to say if these features appeared in addition to the times noted above. These are the dates when they were legibly noted.

fracture, but did reveal spondylosis, patchy opacification, lumbar lordosis, and degenerative changes. Exhibit 1 at 44-45.

A DEXA scan performed on November 11, 2008, showed borderline osteopenia. Id. at 60. A bone density study of the lumbar spine showed compression deformities of the inferior endplates of L3 and L4 and borderline osteopenia in L5. Exhibit 3 at 135.

On December 4, 2008, she was admitted to the hospital for constipation and constant abdominal pain. Id. at 21. An ultrasound of the abdomen suggested fatty infiltration of the liver and gallbladder polyps. Exhibit 1 at 63. A colonoscopy with upper gastrointestinal endoscopy was performed, with results reported as normal. Testing for celiac disease was ordered and later reported negative. Id. at 73. Duodenal biopsies were reportedly unremarkable on December 6, 2008, noting mild reactive gastropathy. Id. at 59.

A barium enema performed on April 3, 2009 showed several diverticuli. Exhibit 3 at 129. Anxiety, insomnia, and frequent bowel movements for three days were noted on October 19, 2009. Stool cultures were obtained. Exhibit 1 at 9-10. A week later, on October 27, 2009, Ms. McCabe was seen for bloody stools and was diagnosed with pinworm and giardia. Id. at 10. A colonoscopy performed on February 18, 2010 and was reportedly "ok." Id. at 10-13. She was diagnosed with irritable bowel syndrome on April 9, 2010. Id. at 11. Acute cystitis and insomnia were noted on June 3, 2010. Id. Insomnia, anxiety, depression, neck pain, chest pain, musculoskeletal pain, bronchitis, gastritis, and tarry stools were noted on July 15, 2010. Id.

Throughout these visits, Ms. McCabe received flu vaccinations on October 2, 2006, September 29, 2007, and October 19, 2009, without any reported problems.[5] Id. at 2, 5, 9.

2. The September 11, 2010 Flu Vaccination and the Following Year

Ms. McCabe visited Dr. Kang on September 11, 2010. Id. at 12. The first notation in Dr. Kang's records from that day records that Ms. McCabe was, again, experiencing fatigue. Id. Dr. Kang also noted gastroesophageal reflux (GERD),

[5] Although there is no record of a flu vaccination for 2008, petitioner's brief reports that Ms. McCabe was certain that she did receive one that year. Pet'r's Pre-Hear'g Br., filed Sep. 11, 2017, at 3.

depression, and anxiety. Id. She was also, again, given a B12 shot. Id. During this visit, Ms. McCabe received a flu shot. Id.

An undated VAERS form, referenced by Sanofi-Pasteur in a letter dated October 25, 2010, identified the site, time, and date of vaccination as right deltoid, at 11:00 A.M. on September 11, 2010. Id. at 93. A VAERS form dated October 22, 2010, memorialized onset of adverse symptoms at 8:00 P.M. on September 11, 2010. The list of adverse occurrences included vision loss, disorientation, unsteady gait, nausea, excessive sleep, and lightheadedness. Id. at 91.

Although the VAERS form suggests an onset of problems on September 11, 2010, Ms. McCabe first sought treatment on September 22, 2010. On that date, Ms. McCabe went to the emergency department of NYU Medical Center for diffuse weakness and malaise. Exhibit 2 at 6. It was noted that Ms. McCabe had received an influenza vaccine yearly for 9 years prior to the vaccination on September 11, 2010. Id. The notes state that she had received the immunization around 11:00 A.M. on September 11, 2010. Id. At about 5:00 P.M., she suddenly began to feel diffusely weak, fatigued, and achy, particularly in her shoulders. Id. She went to bed and slept till 1:45 P.M. the next day. Id. She continued to feel nauseated, lightheaded, and fatigued when she woke up. Id. She reported swelling at the injection site in her left arm and a fever of 101. Id. The notes state that she slept through the day and night and felt sufficiently improved to go to work on Monday, September 13, 2010. Id. "Since then the p[atien]t has had a waxing and waning course of lightheadedness, decreased appetite, woozy feeling, sluggish fatigue with nausea and intermittent h[ead]a[che] and blurred vision but no diplopia. She denies any focal neurological complaints." Id. The ER notes further state that she worked every day and developed a productive cough, nasal pressure, and sinus pain. She had no fever and experienced intermittent chest pressure. Id. She went to the ER on September 22, 2010 because "it was a particularly bad day and she 'felt like I could not function.'" Id.

Medical personnel observed the following: Ms. McCabe's gait was steady, she had normal speech, and she was awake, alert, and oriented according to the nurse's intake. Id. at 19, 28. Her blood pressure was 143/91, heart rate was 81, and she was afebrile. Id. Strength was full and reflexes were symmetrical with downgoing toes. Id.

Dr. Boes, an emergency physician, opined based on these observations:

> 50y[ear] o[old] r[ight] h[anded] f[emale] w[ith] diffuse body aches and weakness w[ith] cough and sinus pressure with many

> constitutional symptoms occurring after a flu shot 10 days ago. P[atient]t's neuro exam [is] normal except for mild Romberg and tandem difficulty which may be near baseline for this p[atien]t who gets regular B12 supplementation. Presentation [is] not suggestive of acute neurological issue but instead c[onsistent] w[ith] viral syndrome or noninfectious inflammation associated in response to the vaccine. Although the p[atien]t's symptoms are often experienced after the flu shot they do not often persist for 10 days.

Id. at 7.

A CT of the brain was read as normal. Exhibit 1 at 95. Chest x-rays showed degenerative changes in the thoracic spine. Id. at 98. Ms. McCabe was discharged later that same day with instructions to return if symptoms worsened. Exhibit 2 at 17, 20.

On September 24, 2010, Ms. McCabe was seen by a neurologist, Dr. Herbstein. Exhibit 1 at 106. She complained of imbalance, her legs feeling weak, intermittent memory issues, and difficulty with daily functioning. Id. She described that "there is a kind of bricks in my head." Id. Dr. Herbstein documented an essentially normal neurological examination. Id.

A brain MRI obtained on that same day showed three punctate hyperintensities in right frontal white matter, which were read as a nonspecific finding. Id. at 100. A vestibular nystagmogram (VNG) showed normal and symmetrical responses to caloric stimulation and normal performance of oculomotor tasks. Id. at 123. Dr. Herbstein noted in a letter dated October 1, 2010, that Ms. McCabe "[s]tates that she slept for a day and afterward she had no memory that slowly started to come back" and that he was "not sure at this point as to what the cause was for the transient neurological dysfunction that she reports." Id. at 110.

Dr. Kang noted on October 2, 2010, that Ms. McCabe reported feeling off-balance and feverish. Dr. Kang diagnosed an upper respiratory tract infection. Id. at 13.

On October 7, 2010, Dr. Herbstein noted that "her neurological examination remains entirely normal with 2/5 symmetrical reflexes, downgoing toes, normal strength, and normal cerebellar examination." Id. at 116. Dr. Herbstein further noted that "Ms. McCabe insists that her symptoms started after she had the flu

shot, but I failed to find any objective abnormalities on my neurological examination." Id.

Also on October 7, 2010, she was seen by Dr. Osterweil, an otolaryngologist. Id. at 131. Ms. McCabe complained of neurological symptoms including vertigo and gait disturbance. Id. Dr. Osterweil reported that VNG, balance tests, and reflex tests indicated no abnormalities. Id. He further reported that he did not associate the MRI hyperintensities to her symptoms. Id. Other than indications of allergic rhinitis and postnasal drip, the exam was reported as unremarkable. Id.

Ms. McCabe also began physical therapy on October 7, 2010. Exhibit 7 at 14. The records show that Ms. McCabe was "ambulating very well without cane" and that "patient's complaints of significant weakness and numbness [are] not consistent with findings for normal gait." Id. Future records from the physical therapist continue to note that Ms. McCabe's reports of having poor balance are inconsistent with her ability to "stop short with minimal loss." Id. at 22, 24, 26, 28.

Between October 11 and October 13, 2010, Ms. McCabe underwent an ambulatory EEG examination. Exhibit 5 at 8. During these exams, patients push a button when they experience a symptom of their condition so that physicians may be able to associate the symptom with certain brain activity. This examination revealed that the 77 push-button events for various neurological complaints reported by Ms. McCabe were not associated with abnormal activity. Id. at 9. However, occasional left anterior temporal sharp waves were noted during sleep and rarely during wakefulness. Id. at 8-9.

On October 19, she was seen again by Dr. Kang, who noted complaints of coughing, headache, ear ringing, decreased memory, and heaviness. Exhibit 1 at 14. Dr. Kang diagnosed acute sinusitis and bronchitis. Id.

Dr. Herbstein noted in a letter dated October 26, 2010, that "[s]he continues to complain of terrible memory issues, unsteadiness, weakness, numbness of the extremities, bone pains, etc. She is convinced that all of this is the result of the flu vaccine. Neurological examination remains within normal limits." Exhibit 6 at 7.

On October 28, 2010, Ms. McCabe saw a pulmonologist, Dr. Chae, for trouble breathing, a cough lasting six weeks, and postnasal drip. Exhibit 4 at 10. Dr. Chae concluded that there was normal pulmonary function and concluded that

her condition was "likely self limited." Id. Four days later, Dr. Chae noted that he had had a follow-up discussion with Ms. McCabe and that "she is feeling a bit better." Id. at 11.

On November 1, 2010, Ms. McCabe was seen by Dr. Forster, a neurologist, for a second opinion of Dr. Herbstein's diagnosis. Exhibit 1 at 132. Dr. Forster noted that since seeing Dr. Herbstein, "she has progressively gotten better." Id. Dr. Forster ultimately concluded that "the current examination is grossly without focal dysfunction" and that he did not think that "beyond the tincture of time and physical therapy there is anything specific that needs to be done." Id. at 133. He concludes "I do think that she suffered a 'viral' illness which must take its course." Id.

Following the visit with Dr. Forster on November 1, 2010, there was an extended period of time without any records of medical treatment or complaints. This gap ends on March 8, 2011, when she returned to see Dr. Forster. Exhibit 8 at 7. Dr. Forster notes: "she is absolutely convinced that the flu vaccine has been the cause of all her symptoms. She complains of loss of memory, pains in legs, swelling of the legs, some blurring of vision, etc. She also reports that she is depressed." Id. Dr. Forster prescribed her Cymbalta and Lyrica. Id. at 8.

Ms. McCabe underwent a neuropsychological evaluation on May 2 and 23, 2011. Exhibit 8 at 15. The evaluation indicated that she performed within the "average range of intellectual and cognitive functioning." Id. at 19. Further, the neuropsychologist noted that her cognitive functioning was "consistent with our estimate of her premorbid level of intellectual functioning." Id. at 20.

Throughout Ms. McCabe's visits in the year following her vaccination, there is no indication that any treating physician associated her ongoing symptoms as being a consequence of the flu vaccine she received on September 11, 2010.

3. From a Year Following Vaccination to Today

Ms. McCabe returned to Dr. Kang for a cough on September 2 and 8, 2011. Dr. Kang diagnosed her with acute bronchitis and general anxiety disorder. Exhibit 1 at 15. On the second visit, Dr. Kang referred her again to Dr. Chae, the pulmonologist. Id.

Ms. McCabe saw Dr. Chae on September 9, 2011, and complained of feeling weak and tired. Exhibit 4 at 2. Again, the medical records note that she stated that

she "[o]verall feels not herself and weaker with leg pains and memory loss since she had the flu shot 9/10." Id. Dr. Chae's records note that Ms. McCabe was being treated for fibromyalgia, although this diagnosis does not appear in Dr. Forster's records. Id. Dr. Chae did not report any significant abnormal findings and noted that the cough seemed to be resolving. Id. He also stated "[s]he is now most concerned with subjective fevers and fatigue." Id.

On a visit to Dr. Kang on December 3, 2011, Ms. McCabe complained of coughing. Exhibit 1 at 16. During this visit, it was noted for the first time that Ms. McCabe's brother has hemochromatosis.[6] Id. Fatigue does not appear to be mentioned, though a B12 shot was administered. Id. Dr. Kang considered acute bronchitis, rhinosinusitis, generalized anxiety disorder, and hemochromatosis as diagnoses. Id.

Beyond December 3, 2011, petitioner's medical records show a number of visits to specialists that do not appear to relate to the present case. These include referrals to an orthopedist (exhibit 1 at 147-48), endocrinologist (exhibit 1 at 154), an otolaryngologist (exhibit 1 at 157-58), a cardiologist (exhibit 1 at 160-61), and a podiatrist (exhibit 1 at 20). Although the undersigned has reviewed these medical records, they do not appear to be material and were not developed at the hearing or in the parties' pre-hearing briefs. They also do not appear to relate to the central issue here, which is petitioner's reported symptoms and diagnoses before and after the September 11, 2010 flu vaccine as they relate to petitioner's putative CFS.

On March 24, 2012, petitioner presented to Dr. Kang complaining of anxiety, cough, stuffy nose, insomnia, leg pain, and GERD. Exhibit 1 at 16. Again, fatigue does not appear to be noted on this visit, although a B12 shot was provided. Id. On April 18, 2012, she presented with depression, insomnia, and a stuffy nose. Id. at 17. Allergic rhinitis, acute rhinosinusitis, depression, insomnia, and GERD were considered as diagnoses. Id.

On June 16, 2012, she presented with shortness of breath, sore throat, and coughing. Id. Again, fatigue was not noted, although a B12 shot was given. Depression and acute bronchitis were also considered. Id.

[6] Hereditary hemochromatosis is a disorder of iron metabolism that is hallmarked by excessive amounts of iron entering the circulatory pool and accumulating in the tissues. Dorland's Illustrated Medical Dictionary 838 (32d ed. 2011).

On July 21, 2012, she presented with shortness of breath and heart complaints. Exhibit 1 at 18. COPD was considered. Id. At this visit, no fatigue was noted and it does not appear that a B12 shot was given. Id. She did wear a Holter monitor for 24 hours, which showed a mean heart rate of 93 and intermittent sinus tachycardia. Id. at 164.

On August 10, 2012, she was seen for a sore throat and burning while urinating. Id. at 18. Fatigue was not noted, although a B12 shot was given. Id. Dr. Kang considered acute cystitis, GERD, anxiety, and allergic rhinitis as possible diagnoses. Id.

She was seen on November 6, 2012, with primary complaints of fatigue and stuffy nose. Id. at 19. Chronic bronchitis, depression, and leg pain were also noted. Id.

On December 17, 2012, Ms. McCabe was seen for shortness of breath, coughing and congestion. Id. Fatigue was not noted, although a B12 shot was given. Id. Dr. Kang considered acute and chronic bronchitis, and anxiety. "Ireland" was noted in the medical records. Id.

On April 2, 2013, she was seen for burning urination and left hip and lower back pain. Id. at 20. Fatigue was not noted, although a B12 shot was administered. Id.

On May 18, 2013, she was seen for a swollen left foot. Id. Though fatigue is not noted, insomnia is noted and a B12 shot was administered. Id. COPD was also considered among the diagnoses. Id.

On May 25, 2013, menopause was noted in the medical records for the first time. Exhibit 100 at 15. She was prescribed Prozac, with the notation that it may have been "for menopause." Id. Fatigue was not noted, and no B12 shot was administered. Id.

On July 13, 2013, she presented with insomnia, anxiety, and coughing. COPD, anxiety, rhinitis, and GERD were considered as diagnoses. Id. No report of fatigue was made and it does not appear that a B12 shot was given. Id.

On August 16, 2013, she presented with coughing, which produced yellow sputum. Id. She noted being both cold and warm. Id. Fatigue was not noted,

although a B12 shot was administered. Id. Acute bronchitis, rhinitis, and COPD were noted. Id.

On September 28, 2013, she was seen for neck pain and shortness of breath. Id. at 14. While the records from this date are especially difficult to read, again fatigue was not apparently noted, but a B12 shot was administered. Id. COPD and chronic bronchitis were noted in the records. Id.

She was seen on December 6, 2013, though the notes are again especially difficult to decipher for this visit. Id. at 13. The presenting issue appears to be related to stomach pain, and GERD was noted. Id. Fatigue does not appear to be noted and a B12 shot does not appear to have been administered. Id.

On February 4, 2014, she was seen for a nasal allergy and a cough that produced sputum. Id. at 12. Acute bronchitis, COPD and depression were noted. Id. Fatigue was not noted, although a B12 shot was administered. Id.

On April 3, 2014, a retroesophageal subclavian artery was noted.[7] Id. at 11. COPD, depression and anxiety, and rhinitis were also considered. Id. Fatigue was not noted. While it appears that Ms. McCabe requested a B12 shot, whether it was administered is not clear.

On June 2, 2014, she presented with anxiety, COPD, and shortness of breath. Id. at 10. COPD, anxiety, and depression were recorded as diagnoses. Id. No mention is made of fatigue or a B12 shot. Id.

On June 30, 2014, anxiety, palpitations and tachycardia, and COPD were noted in her records. Id. at 9. Sinus tachycardia, anxiety, COPD, and depression were considered as diagnoses. Id. No note of fatigue is found in the record, though a B12 shot was given. Id.

On September 20, 2014, she presented complaining of shortness of breath, coughing, depression, and anxiety. Id. at 8. Acute bronchitis, COPD, anxiety, and depression were considered. Id. There is no note of fatigue, although a B12 shot was given. Id.

[7] As its name suggests, a retroesophageal subclavian artery is a congenital defect where the subclavian artery passes behind the esophagus, instead of in front of it. Tr. 690.

On October 30, 2014, she presented complaining of leg and foot pain, short term memory loss, and concentration deficits. Id. at 7. Dr. Kang considered dysphagia, anxiety, menopause, insomnia, and COPD. Id. There is no mention of fatigue, although a B12 shot was given. Id.

On December 11, 2014, she presented with acute glaucoma, stuffy nose, and coughing. Id. at 4. Acute bronchitis, acute rhinosinusitis, COPD, anxiety, and insomnia were noted. Id. There is no mention of fatigue, although a B12 shot was noted as requested. Id. The records do not indicate if it was given. Id.

On February 17, 2015, she presented complaining of coughing. Id. at 3. Acute bronchitis, COPD, anxiety, insomnia, and GERD were considered as diagnoses. Id. No note of fatigue or a B12 shot is found in the record. Id.

On March 20, 2015, Ms. McCabe began seeing Dr. Malik Megjhani following Dr. Kang's retirement. Id. at 24; Tr. 121. Fortunately, Dr. Megjhani kept legible records. On that day, Ms. McCabe presented with a chief complaint of cold, cough, shortness of breath, and cold sweats. Exhibit 100 at 24. She also reported general malaise. Id. She was diagnosed with an upper respiratory infection, COPD, and allergic rhinitis. Id. No fatigue was noted, though a B12 shot was administered. Id.

On April 11, 2015, she saw Dr. Megjhani for a prescription renewal. Id. at 27. No other complaints were noted other than pain in her left foot. Id. Dr. Megjhani noted "no systemic symptoms" and maintained an assessment that included allergic rhinitis, COPD, GERD, insomnia, and anxiety. Id. She also states that she wanted to be tested for hemochromatosis because her relatives have it. Id. There was no note of fatigue or a B12 shot. Id.

On April 14, 2015, she had an appointment for the purposes of getting blood work done. Id. at 30. She requested and received a B12 shot, though no note of fatigue was made. Id. She also reported that she was not experiencing malaise or any other systemic symptoms. Id.

On August 8, 2015, she was seen in an office visit by Dr. Min Young Kim. Id. at 37. Her chief complaint was left shoulder pain and she requested a prescription renewal. Id. The records note that she is "doing well no complaints" and has "no intercurrent health problems." Id. Dr. Kim assessed her with COPD, GERD, insomnia, and shoulder pain. Id. at 39.

On September 10, 2015, she complained of a sore throat. Id. at 41. She otherwise stated that she was not experiencing malaise. Id. There was no report of fatigue, but a B12 shot was administered. Id.

On February 2, 2016, she presented with a chief complaint of a cough and requesting a prescription refill. Id. at 45. She reported that she is not experiencing malaise. Id. No note of fatigue is made, though she is assessed with insomnia, an upper respiratory infection, and B12 insufficiency. Id.

On March 31, 2016, she presented for a prescription refill and a B12 injection. Id. at 49. She also noted her ongoing anxiety and insomnia. A battery of labs was ordered to address her fatigue. Exhibit 11 at 52.

On May 27, 2016, she presented for a prescription refill. Exhibit 100 at 53. She also complained of chronic nasal congestion and snoring at night. Id. No systemic symptoms were reported. Id. She was given a shot of B12, though the record does not note fatigue. Id. For this visit she was referred to an ENT, physical therapist, and a sleep study. Id. This is the first of, at least, two times that Ms. McCabe was referred for a sleep study. According to her testimony, she has never completed the ordered sleep study. Tr. 127. The ENT diagnosed her with chronic sinusitis and granulomatous disease.[8] Exhibit 100 at 61.

On July 16, 2016, she presented for a B12 shot and a prescription refill. Id. at 57. In this visit she complained of nasal congestion, shortness of breath, and fatigue. Id.

On September 8, 2016, she presented for her annual physical. Id. at 61. She complained of a dry cough and also requested a B12 shot. Id. No other symptoms, including fatigue, were noted. Id. During this physical, she was given a patient health questionnaire. She was asked if, over the past two weeks, she experienced (1) "Little interest or pleasure in doing things" or (2) "Feeling down, depressed, or hopeless?" She responded "no" to both. Id. at 64.

[8] Granulomatous disease is an immune disorder caused by dysfunction of certain immune cells that protect the body from infections. The disease is characterized by frequent infections, particularly pneumonia and other infections of the lung. Chronic Granulomatous Disease, Mayo Clinic (accessed May 10, 2018), https://www.mayoclinic.org/diseases-conditions/chronic-granulomatous-disease/symptoms-causes/syc-20355817.

On September 30, 2016, she was seen by Dr. Eugene Shostak, based on a referral from Dr. Megjhani. Id. at 126. Dr. Shostak noted that Ms. McCabe was being seen for a chronic cough, lasting five years. Id. He notes that she stated that "[s]he has never had any prior breathing problems until she got a flu shot and developed a severe allergic reaction requiring admission to NYU Langone Medical Center. Since then her cough never stopped." Id. He stated "[s]he denies fever, chills, malaise, fatigue, weight loss." Id. Dr. Shostak referred Ms. McCabe to Dr. Michael Chandler, since Dr. Shostak's assessment of her condition was that sinusitis was the cause of her problem. Id. at 128.

On October 16, 2016, she was seen by Dr. Chandler. Id. at 129. Dr. Chandler diagnosed right sphenoid sinusitis and an infected nasopharyngeal cyst. Id. at 133. He concluded that these conditions were consistent with her laryngospastic symptom patterns. Id. at 133. His overall impression was "[l]ow-grade background of allergy with isolated sphenoid sinusitis and a complex architecture of her nose with a significant leftward septal deviation." Id.

On November 7, 2016, she presented to Dr. Megjhani for a prescription refill and also requested a B12 shot. Id. at 68. She complained of chronic nasal congestion and snoring at night. Id. No other systemic issues were identified. Id. at 69.

On December 19, 2016, she presented with a chief complaint of cough and nasal congestion. Id. at 72. She also reported experiencing malaise. Id. She was assessed with allergic rhinitis, primary insomnia, and anxiety disorder. Id.

On January 21, 2017, she presented with a chief complaint of chest pain, shortness of breath, sore throat, cough, and fatigue. Id. at 75. She was assessed with an upper respiratory infection. Id. at 77.

On February 15, 2017, she presented to Dr. Zaza Aivazi with a chief complaint of chest pain and cough. Id. at 79. Dr. Aivazi assessed her with mitral regurgitation, tricuspid regurgitation, COPD, prediabetes, and anxiety disorder. Id. at 82.

On April 18, 2017, she was seen for a prescription renewal and B12 shot. Id. at 170. At the renewal, she reported still experiencing anxiety and difficulty falling asleep. Id. Otherwise she was reported as having no apparent disease. Id. She was assessed with anxiety disorder, insomnia, allergic rhinitis, and GERD. Id. at 171.

In the last visit in the records, on September 11, 2017, she was seen with a primary complaint of shortness of breath, pain in her foot, feeling tired, and losing weight. Id. at 173. During the evaluation, Ms. McCabe reported that "she developed leg edema, burning sensation in the feet, snoring, [shortness of breath] and other chest issues only after getting flu shot." Id.

Though the record indicates that Ms. McCabe would sometimes state to her treating physicians that the flu vaccine was the cause of all her symptoms, in the seven years of medical records following the vaccination there does not appear to be a single treating physician that documented a belief that the vaccine was the cause of Ms. McCabe's ongoing condition.

B. Ms. McCabe's Testimony

Ms. McCabe testified that she was born in Ireland and moved to New York City around 1982, where she resides now. Tr. 13-14. She had, approximately, a 9th grade education. Tr. 12; exhibit 8 at 14. When she moved to the United States, she first worked as a waitress. Tr. 14. Around that time, she became a U.S. citizen and she trained to become a nurse's aide. Tr. 16. After receiving her certification, she began a career as a full-time in-home aide. Tr. 16-17. She continued in this career up and through the time of the September 11, 2010 vaccination.

Ms. McCabe stated that "[e]verything was great" when asked what her life was like prior to the vaccination. Tr. 17. "[E]verything was just 100 percent." Id. She reported that prior to the vaccination she liked to hike, play ping pong, go on walks, "parties, had a lot of good friends, go to showers, weddings, all that stuff, participate, like I enjoyed my life." Id. She later added "I was very active. I was able to be out and about. Everybody would think I was, like, a wind machine. I was running all over the place, and I'd go to all the events. I would go out walking. I would help people out. I would remember. I had memory that was unbelievable." Tr. 26.

When petitioner's attorney asked if the history of fatigue, depression, COPD, GERD, anxiety, and insomnia affected her life before the depression, she said "No." Tr. 18. She noted that "I was taking medication, but I was doing okay." Id.

In her testimony, Ms. McCabe's counsel elicited additional details on her previous activities:

Q. And you said that you were hiking. I think these were things that you mentioned in your –

A. Hiking, yeah.

Q. Can you describe what you mean by "hiking"? What's the difference between hiking and walking?

A. Like in the woods. I would be out in the woods and going to the lakes and -- you know...

Q. And you were going to parties and dancing. Was dancing one of your favorite things –

A. Dancing was one of my favorite things. I loved to dance, yes. It was one of my favorite things, and I enjoyed going to Broadway shows, and I would be swinging around at the Broadway shows. I loved to dance, yes.

Tr. 27-28.

During her direct testimony, Ms. McCabe did present some testimony to explain her previous reports of insomnia and depression in the medical records. In her early testimony she stated that while she experienced these symptoms, they were not significant and did not adversely affect her.

Specifically, when asked about the significance of her depression prior to the vaccination she answered: "Well, basically I think it was to do with – the depression was basically to do with menopause, I think, that's why I was on depression pills." Tr. 20.

Ms. McCabe similarly indicated that the insomnia she experienced used to be different than it is now. Before the vaccination, she testified that "I just couldn't sleep great at nights, but I did take Ambien, and I would wake up the next morning fully refreshed." Tr. 21. Similarly, she indicated that her fatigue did not present her with any problems:

Q. Did your fatigue cause you any problems with work or any of your activities that you described?

A. At that time?

Q. Yeah.

A. No, no, because I would be sleeping at night, so I was able to go.

Tr. 21.

However, on cross-examination she appeared to shift towards stating that her condition prior to the September 11, 2010 vaccinations may not have been minor but instead reflected adverse reactions to earlier vaccinations:

Q. The reason I ask is Dr. Kang's medical records for those same periods of time I mentioned in Exhibit 1, page 1 through 7, repeatedly talk about depression and insomnia.

A. Well, I guess they call it that if you don't sleep, insomnia, right?

Q. That's what he called it.

A. I don't know. I don't know the medical terms.

Q. But you --

A. Which year was that?

Q. 2006 and 2007, 2008.

A. Yeah. I was taking flu vaccines all of that time.

Tr. 64-65.

In describing her current medical condition, Ms. McCabe stated that "[m]y whole life has changed. My whole life has just been turned upside down. It's like I'm a different person. I don't get out as much as I used to. I don't dance anymore. I had swelling all over my legs. I have still pains in my legs. I still am getting colds on a constant basis." Id.

When asked how she is when she wakes up from being able to sleep, Ms. McCabe stated "I have insomnia, so I can't – I could take an Ambien and I could be awake all night." Tr. 41. Again, in describing her current sleep patterns, Ms. McCabe contrasted her current condition with her condition before the vaccine: "I was never like this. I was always on the go. It would take a lot to hold me down.

Now, my whole life is just a complete nightmare. It's been a nightmare for the last six years, a nightmare." Tr. 41.

Ms. McCabe stated that she was no longer able to work full-time as a nurse's aide following the vaccination. Tr. 41. She did, however, work the week before going to the ER on September 22, 2010. Exhibit 2 at 10; Tr. 62. She also appeared to not stop working as a secretary at Wankel hardware. See Section IV.B.1. In her testimony, she stated that she went back to work as a nurse's aide two years after the flu vaccination. Tr. 61. She further stated that she has since been able to work part-time, intermittently. Id. She stated that today she works "two, three days a week." If she's too tired, she doesn't work. Tr. 42.

Ms. McCabe testified that prior to receiving the flu vaccine in question, she spoke with a nurse who had had an adverse reaction to the flu vaccine. Tr. 51-52. This conversation led Ms. McCabe to conclude that she herself had an adverse reaction to the flu vaccine. Specifically, she recalls herself thinking: "Oh, Lily had a reaction. Could this possibly be a reaction to the flu vaccine?"

The undersigned will return to evaluate the factual history and Ms. McCabe's testimony as it relates to her diagnosis in Section IV.B.2, below.

II. Procedural History, Including Presentation of Expert Reports

Ms. McCabe's case has been pending for several years. As set forth in more detail below, the case's prolonged duration is attributed, in large part, to Ms. McCabe's multiple changes in her theory of the case. Ms. McCabe initially was proceeding on a claim that the flu vaccine caused a demyelinating condition. After the parties explored whether Ms. McCabe suffered a demyelinating injury, she switched to asserting that the flu vaccine caused cytokine release syndrome (CRS). When pressed to support this theory with reliable evidence, Ms. McCabe presented yet another claim: that the flu vaccine caused her to develop CFS. Later, Ms. McCabe slightly adjusted her theory of the case again by advancing the alternative cause of action that the flu vaccine significantly aggravated her pre-existing CFS.

These separate stages are set forth below. The backbone of Ms. McCabe's case are the collection of expert reports. Thus, the reports from Dr. Axelrod, Ms. Mikovits, and Dr. Levine are presented in some detail. Additionally and importantly, the Secretary's response to those reports and the undersigned's orders for more information provide context for the subsequent reports from Ms. McCabe's experts.

A. Ms. McCabe's Initial Claim: A Demyelinating Injury

Ms. McCabe filed her original petition on August 12, 2013. Her original petition does not allege a specific injury, but instead claims she suffered "health issues" as a result of the vaccine received on September 11, 2010. Pet. at 1. She filed her statement of completion on October 16, 2013, and respondent reported that the medical records filed were sufficiently complete. Resp't's Status Rep., filed Nov. 14, 2013, at 1. The undersigned then set a deadline of January 10, 2014, for the respondent's Rule 4(c) report. Order, issued Nov. 18, 2013.

The undersigned extended the deadline for respondent to file his Rule 4(c) report to March 21, 2014, due to missing medical records. Order, issued Feb. 10, 2014. Respondent timely filed his Rule 4(c) report on March 21, 2014. A status conference was held on March 31, 2014, to discuss the contents of this report and the next steps. The possibility of settlement and the need for additional employment records were also discussed. Order, issued Apr. 2, 2014. In a later status report, respondent stated that settlement would not be possible unless the petitioner amended her petition to identify the specific injury she alleges the vaccine caused. Resp't's Status Rep., filed July 8, 2014.

A status conference was held on August 18, 2014, to discuss the need for an amended petition and additional medical records. Following the conference, the undersigned ordered the petitioner to file her amended petition by October 2, 2014. Order, issued Aug. 19, 2014. Petitioner was ordered to identify what injury the vaccine caused. Id.

On October 2, 2014, petitioner filed her amended petition, stating that the flu vaccine caused "an aggravation of a pre-existing demyelinating condition." Am. Pet. at 1. A status conference was held on October 8, 2014, to discuss the amended petition. Following the status conference, petitioner was ordered to file an expert report in 60 days. Order, issued Oct. 9, 2014. Ms. McCabe filed a report from Dr. Axelrod on October 27, 2014. Exhibit 16.

1. Dr. Axelrod's Background and First Report

a. Dr. Axelrod's Qualifications

When he submitted his report, Dr. David Axelrod was a clinical immunologist and Associate Professor with the Oakland University - William Beaumont School of Medicine in Royal Oak, MI. Dr. Axelrod received an undergraduate and medical degree from the University of Michigan. He also received a Masters from the University of Michigan School of Public Health. He

states that when he worked as principal investigator at the Walter Reed Army Institutes of Research in 1982-1984, his laboratory participated in vaccine development.

b. Dr. Axelrod's First Report (Exhibit 16)

Dr. Axelrod ultimately did not testify in this matter. However, a brief review of the contents of his report is helpful in two ways. First, it demonstrates how petitioner's other experts adopted portions of his report in making their conclusions. Second, it provides important context for understanding rebuttals made by respondent's experts.

Dr. Axelrod states that the "objective findings suggest dysfunction of parts of her nervous system. This dysfunction was caused by an immune response to the vaccine that resulted in damage/dysfunction of her central nervous system, including demyelinating disease." Exhibit 16 at 1.

To support his theory, Dr. Axelrod cites articles that, he says, show that vaccination will cause elevated levels of certain compounds, including interleukin-6 (IL-6), which will persist in time. Id. at 2-3. These compounds will, according to Dr. Axelrod, lead to disruption of the blood brain barrier, allowing blood-borne chemicals to enter and affect the brain. Id. Dr. Axelrod opines that these chemicals resulted in her anxiety, depression, and the new brain demyelinating disease that can be associated with the symptoms she experienced following the September 11, 2010 flu vaccine. Id.

A status conference was held on November 3, 2014, to discuss Dr. Axelrod's report. On respondent's request, respondent was provided 60 days to evaluate the report to determine whether settlement was possible. Order, issued Nov. 4, 2014. On January 5, 2015, respondent stated that he would be submitting a report from Dr. Leist in rebuttal to Dr. Axelrod's report. Resp't's Status Rep. Respondent filed Dr. Leist's report on February 20, 2018. Exhibit A.

2. Dr. Leist's Background and First Report

a. Dr. Leist's Qualifications

Dr. Thomas Leist is a neurologist and Professor of Neurology with Thomas Jefferson University in Philadelphia, PA. Dr. Leist received his diploma and Ph.D. in Biochemistry from the University of Zurich and his M.D. from the University of Miami. He now serves as the Chief of the Division of Clinical Neuroimmunology and the Director of the Comprehensive Multiple Sclerosis Center.

b. Dr. Leist's First Report (Exhibit A)

Dr. Leist's initial expert report provides a comprehensive review of Ms. McCabe's medical history, which was used as a basis for subsequent expert's reports. Exhibit A at 1-7.

Dr. Leist addresses each of the articles referenced by Dr. Axelrod and raises a number of concerns about each. Id. at 7-8. However, it is not necessary to go into great depth here given that petitioner decided not to rely on Dr. Axelrod's opinion and accompanying articles.

Dr. Leist then presents his opinion in this matter. Id. at 9. He points out that Ms. McCabe's alleged neurological symptoms began at approximately 4:30 P.M. (when she alleged that she "felt so tired" and "could not stand up.") Id. at 10. This was approximately five hours after receiving the flu vaccine. He opines: "A four to five hour time interval between vaccination and symptom onset is too short to allow occurrence of such a cognate process that as Dr. Axelrod opines: 'resulted in damage/dysfunction of her brain related to her anxiety and depression or the damage/dysfunction of her brain resulted in a new brain demyelinating disease.'" Id. On the other hand, Dr. Leist opines, her symptoms were fully consistent with an upper respiratory tract infection. Id.

Further addressing whether Ms. McCabe experienced a focal neurological insult following the vaccination, Dr. Leist points out that examinations by several different practitioners did not identify any focal findings. Id. Among these were neurological examinations by Dr. Herbstein (exhibit 1 at 106), the NYU emergency department (exhibit 2 at 7), Dr. Forster (exhibit 8 at 8), and Dr. Sivak (exhibit 8 at 11).

As a result, Dr. Leist ultimately concludes that the influenza vaccine Ms. McCabe received on September 11, 2010 "did not cause, contribute to, or worsen the various health conditions from which Ms. McCabe suffered before and after September 11, 2010." Exhibit A at 11. He further notes that "Ms. McCabe did not experience a demyelinating central nervous system injury or aggravate a preexisting central nervous system injury as a result of the influenza vaccination she received on September 11, 2010." Id.

A status conference was held on March 2, 2015, to discuss Dr. Leist's report. During the status conference, petitioner was given until April 10, 2015, to file a responsive report from Dr. Axelrod. Order, issued Mar. 3, 2015. Dr. Axelrod's report was timely filed on March 19, 2015. Exhibit 30.

3. Dr. Axelrod's Second Report (Exhibit 30)

In his supplemental report, Dr. Axelrod again cites several articles in support of his claim that vaccination results in elevated levels of certain compounds that can cause damage to individuals' nervous systems. Exhibit 30 at 1. He further states that the effect of these compounds could be part of a primary immune response or part of a secondary immune response. Id. at 2-3. Thus, the vaccination could explain both her immediate symptoms and her symptoms that developed in the days and weeks following the vaccination. Id.

* * *

In a status conference on March 30, 2015, the undersigned raised the concern that Dr. Axelrod's report did not address the issue of significant aggravation, which was alleged in Ms. McCabe's amended petition. Order, issued Mar. 30, 2015. Respondent also requested an opportunity to review and comment on Ms. McCabe's MRI images. Id. Ms. McCabe was ordered to produce the images from the MRI so that respondent's expert could evaluate them. Id.

4. Change in Counsel and Change in Theory

During a status conference held on May 27, 2015, petitioner's counsel of record stated that he intended to transfer the case to substitute counsel. Order, issued May 28, 2015. Substitute counsel entered an appearance on August 13, 2015. A status conference was set for August 27, 2015. During the status conference, the parties reviewed the case with petitioner's new attorney and revisited the issue of the missing MRI images. Order, issued Aug. 27, 2015. Petitioner also stated that she intended to have a neurologist provide an opinion. Id. The undersigned set a deadline of October 28, 2015, for the neurologist's report. Id.

Petitioner sought, and was granted, enlargements of time to file the report from a neurologist on October 26, 2015, and December 28, 2015. Orders, issued Oct. 27, 2015, and Dec. 29, 2015. Petitioner filed a third motion for an enlargement of time to file the neurologist's report on January 28, 2016. The undersigned deferred ruling on this third motion until after a status conference was held on February 3, 2016, to discuss the reason for the delay in procuring the report. Order, issued Jan. 29, 2016. Petitioner's motion was granted following the status conference. Order, issued Feb. 4, 2016. Petitioner then filed a fourth motion for an enlargement of time to file the neurologist's report on February 29, 2016. This motion was granted. Order, issued Mar. 2, 2016. Petitioner then filed a fifth

motion for enlargement of time on April 13, 2016. This motion was also granted. Order, issued Apr. 14, 2016.

On June 14, 2016, petitioner moved for a sixth enlargement of time to file her expert report. However, in this motion, Ms. McCabe stated that the neurologist from whom she had planned to procure the report had concluded that petitioner should have an expert in ME/CFS and fibromyalgia review the records, not a neurologist. Pet'r's Mot. at 1. The undersigned deferred ruling on this motion until following a status conference, which was, after being delayed, held on June 29, 2016. Order, issued June 15, 2016. During the status conference, Ms. McCabe informed the undersigned that an expert report would be filed imminently and respondent requested 60 additional days to file a responsive report. Order, issued June 29, 2017. Petitioner filed a report from Ms. Mikovits the next day. Exhibit 40.[9]

B. Petitioner's Second Claim – Cytokine Release Syndrome

1. Ms. Mikovits' Background and First Report

a. Ms. Mikovits' Qualifications

Ms. Judy Mikovits is a consultant with MAR Consulting Inc. She earned an undergraduate degree in chemistry from the University of Virginia and a Ph.D. in biochemistry from George Washington University. Ms. Mikovits did not attend medical school and is not a licensed medical doctor.

b. Ms. Mikovits' First Report (Exhibit 40)

In her first report, Ms. Mikovits puts forth that cytokine release syndrome (CRS) is an immune related adverse event seen in a number of immune compromised patients receiving checkpoint inhibitors. Exhibit 40 at 2. She cites T.J. Williams et al., Association of Autoimmune Encephalitis With Combined Immune Checkpoint Inhibitor Treatment for Metastatic Cancer, 73 J. Am. Med. Assoc. Neurology 928 (2016)[10] to support this claim. Ms. Mikovits further notes that CRS can occur within hours of "treatment" and can be diagnosed by high levels of several molecules, including IL-6, CRP, ferritin, and lactate. Exhibit 40 at 2. By discussing checkpoint inhibitors in the context of a claim that the flu

[9] Ms. Mikovits co-authored reports with Francis Ruscetti. However, Ms. Mikovits testified and Mr. Ruscetti did not. Therefore, for ease of reference, this decision identifies the reports as coming from Ms. Mikovits.

[10] Petitioner did not file this article into the record.

vaccine harmed Ms. McCabe, Ms. Mikovits implies that checkpoint inhibitors are somehow similar to a flu vaccine, but fails to establish or to explain how. Id.

Ms. Mikovits then cites a 2011 blog post for the proposition that there have been fatal reactions to Rituxan immunotherapy. Id. (citing Rituximab [Rituxan] – Fatal Infusion Related Reactions in Patients with Rheumatoid Arthritis, THERAGENOMICS BLOG (June 6, 2011), https://thassodotcom.wordpress.com/2011/06/07/rituximab-rituxan-fatal-infusion-related-reactions-in-patients-with-rheumatoid-arthritis/). Again, she implies that there is a reason to connect Rituxan treatment to the flu vaccine, but she makes no attempt at connecting the two. See exhibit 40 at 2.

Ms. Mikovits then points out that COPD, which Ms. McCabe had, is an inflammatory disorder and further states that individuals with COPD have an altered lung microbiome. Id. at 2-3. She continues, without support, to say that "it is likely that vaccine induced changes in the intestinal microbiome can exacerbate COPD symptoms." Id. at 3. She then notes that "a balance of the gut-lung axis is critical to clearance and response to Influenza." Id. It is not clear whether she was referring to an influenza virus or influenza vaccine.

Ms. Mikovits opines that administrations of influenza vaccine prior to the September 2010 administration were responsible for Ms. McCabe's preexisting history of depression, fatigue, and insomnia. Id. She notes, without support, that each of these three disorders is "firmly associated with elevated levels of the pro-inflammatory cytokines like IL6 and the development of serious even fatal anaphylactic reactions even after several course[s] of treatment with the immune therapy." Id. Ms. Mikovits' references to anaphylactic reactions appears misplaced as no evidence of anaphylaxis appears in Ms. McCabe's medical records.

Ms. Mikovits then asserts that Ms. McCabe was always ill and should not therefore have been vaccinated when ill. Id. However, Ms. Mikovits provides no support or logical basis for this assertion. She continues: "The diagnoses of chronic multi-cystic thyroiditis and COPD showed that she was predisposed toward autoimmunity making rapid timing for cumulative autoimmune reactivity more likely in 2010." Id. Ms. Mikovits goes on to argue that Ms. McCabe suffered injuries after each vaccination, noting that "immediate reactivity (e.g. hives, eczema, angioedema [and] wheezing) occur rarely after influenza vaccination (all types), but occurred in every instance of Ms. McCabe's flu vaccinations since 2007." Id. at 4-5. However, the bases for Ms. Mikovits' assertions are not provided. She goes on to note that Ms. McCabe's reactions got

"cumulatively worse leading to anaphylaxis-like reaction." Id. at 5. It is not clear in what way Ms. McCabe's reactions to the vaccine were anaphylactic or "anaphylaxis-like." It is also not clear what "anaphylaxis-like" means. Ms. Mikovits' willingness to offer a diagnosis not in the record is troubling given that she is not medically qualified.

Ms. Mikovits states that Ms. McCabe "had an immediate and sustained reaction developing coughing and wheezing by January 6, 2007 indicating a dysregulation of the lung microbiome and vasculitis and small airway disease." Id. She continues to say that all these symptoms are consistent with "damage of gut-lung microbiome and immunotherapy / vaccine-induced cytokine release syndrome." Id. Ms. Mikovits does not distinguish symptoms that pre-existed the vaccination from symptoms Ms. Mikovits is associating with cytokine release syndrome. As Ms. McCabe testified, she had experienced the chronic cough since her youth. Tr. 24. It is not clear if Ms. Mikovits was aware of this fact. Furthermore, Ms. Mikovits does not provide any scholarship to support the concept of "vaccine-induced cytokine release syndrome." See exhibit 40 at 5.

Ms. Mikovits proceeds to claim that Ms. McCabe's symptoms throughout the summer of 2007 constituted a "worsening of inflammatory / autoimmune symptoms and evidence of lymphatic dysregulation." Id. Again, this claim is given little weight because Ms. Mikovits has not identified any doctor who diagnosed Ms. McCabe with "lymphatic dysregulation." Moreover, Ms. Mikovits has not explained why she is qualified to come up with this diagnosis on her own. In any event, Ms. Mikovits reviews Ms. McCabe's symptoms from 2007 to 2010, remarking along the way that "considering the multi-focal inflammatory sequelae and disease symptoms, it was medically inadvisable to give her an influenza vaccine on September 11, 2010." Id. Again, Ms. Mikovits seems to be straying from her area of expertise when she offers not only medical conclusions, but also questions the actions of treating physicians.

After reviewing Ms. McCabe's medial history, Ms. Mikovits returns to summarize that "[i]t is our contention these previous vaccines were not without injury primarily encephalopathy (brain inflammation) as well as gut/urinary tract issues and respiratory tract issues." Id. at 6. Ms. Mikovits did not identify any records showing when Ms. McCabe experienced brain inflammation. In the absence of a medical doctor's diagnosis of brain inflammation, it is not clear what factual basis or qualifications Ms. Mikovits has to make this diagnosis.

Ms. Mikovits then summarizes Ms. McCabe's symptoms following the administration of the vaccine and noted that "all of these symptoms are consistent

with Cytokine Release Syndrome (CRS) and damage mediated by cytokines including IL-6." Id. She goes on to state that the symptoms "can be the result of cumulative autoimmunity resulting from molecular mimicry of tetra and pentapeptides cross reacting with self-proteins, including myelin basic protein as recently detailed with H5N1 influenza vaccine." Id. To support this proposition she cites D. Kanduc, Peptide Cross-Reactivity: The Original Sin of Vaccines, 4 Frontiers Biosciences 1393 (2012).[11]

Listing more symptoms (lightheadedness, decreased appetite, wooziness, sluggishness, and intermittent headache), Ms. Mikovits concludes that these clinical symptoms are "consistent with CRS and hypothalamic neurodegeneration mediated by changes in the gut microbiome and aberrant trafficking of innate immune cells to the CNS via brain lymphatics and a leaky blood brain barrier." Exhibit 40 at 6. Again, Ms. Mikovits has identified no medical doctor to corroborate her opinion that Ms. McCabe suffered from "hypothalamic neurodegeneration."

Ms. Mikovits also reviews the opinion presented by the emergency room physician, Dr. Boes. Dr. Boes had concluded Ms. McCabe's "presentation is not suggestive of acute neurological issue but instead consistent with viral syndrome or noninfectious inflammation associated in response to the vaccine." Id. (citing exhibit 2 at 6). Ms. Mikovits points out that "[b]y definition, this is a vaccine injury as non-infectious inflammation of the brain is the definition of encephalopathy." Exhibit 40 at 7.

Ms. Mikovits proceeds to rebut the physician's claim that Ms. McCabe did not have an acute neurological condition by stating that this conclusion was "refuted just two days later by an MRI" which showed three punctate hyperintensities in right frontal matter. Id. While Dr. Herbstein, the neurologist that ordered the MRI, concluded that the findings were "nonspecific" for "multiple etiologies," exhibit 1 at 100, Ms. Mikovits uses the hyperintensities and the results of Ms. McCabe's October 2010 EEG to conclude that Ms. McCabe suffered from "vaccine-causing brain pathology, even if it was not an obvious acute encephalopathy." Exhibit 40 at 7. To be sure, Ms. Mikovits is challenging the medical diagnosis of Dr. Boes, the emergency department physician, by disagreeing with the interpretation of Ms. McCabe's EEG and MRI made by Dr. Herbstein, Ms. McCabe's treating neurologist. She does all this without ever even seeing the EEG or MRI that formed the basis for Dr. Herbstein's diagnosis.

[11] Petitioner did not file this article into the record.

Ms. Mikovits then reviews Ms. McCabe's various symptoms through the month of October 2010. Id. Specifically, she references acute sinusitis and bronchitis, reports of memory loss, unsteadiness, weakness, numbness, and bone pains. Id. Ms. Mikovits states, again without support, that all are consistent with cytokine release syndrome and overexpression of IL-6. Id. She then states that Ms. McCabe's treatment with prednisone supports a diagnosis of CRS. Id. However, this logic does not seem to follow since Ms. Mikovits is attempting to infer the diagnosis based on the prescription and not on the actual diagnosis Ms. McCabe was given. No evidence in the record indicates that the physicians prescribed prednisone to treat CRS as opposed to other inflammatory conditions Ms. McCabe was experiencing.

Ms. Mikovits notes that Ms. McCabe's symptoms continued into 2011 and criticizes her physicians for not having performed testing that would demonstrate that Ms. McCabe had myalgic encephalomyelitis (ME), chronic regional pain syndrome (CRPS), or fibromyalgia (FM). Exhibit 40 at 7.

Ms. Mikovits then states that "recent publications concerning molecular mimicry following influenza vaccine and brain lymphatics are critical to the progressive encephalopathy and hypothalamic brain degeneration and peripheral neuropathy experienced by Ms. McCabe after each influenza vaccine since 2007 with the final blow being the Flu vaccine of 2010." Id. at 8. Ms. Mikovits did not identify any record in which a medical doctor diagnosed Ms. McCabe as suffering from encephalopathy or hypothalamic brain degeneration. So, it appears that Ms. Mikovits is diagnosing these conditions. It is not clear what factual bases support this conclusion and it is concerning to the undersigned that Ms. Mikovits is, again, diagnosing Ms. McCabe's condition without sufficient expertise to do so.

Ms. Mikovits states that the 2010 Sanofi flu vaccine contained a "new B antigen" and associates this B antigen with the development of narcolepsy through molecular mimicry. Id. at 8. Ms. Mikovits does not explain the relevance of narcolepsy in Ms. McCabe's case. Ms. Mikovits then concludes "thus, because of her immune compromised state at the time of inoculation, novel molecular mimicry and cross reactive epitopes could have resulted in the anaphylactic response with the symptoms occurring within hours." Id. Again, it is not clear what in the record Ms. Mikovits is referring to in relation to this "anaphylactic response."

Ms. Mikovits concludes that:

> Ms. McCabe's history of abdominal complaints, nausea and vomiting, gastric reflux, diverticulosis, and urinary tract infections preceding and following each flu vaccination had cumulative effects that allowed rapid brain injury occurrence after six hours in contrast to Dr. Leist's assertion to the contrary. These chronic GI symptoms had already altered the blood brain barrier so that rapid microglia activation released cytokines and chemokines as well as an influx of inflammatory stimuli. There are many examples of fatigue and cerebral dysfunction caused by these stimuli. Thus, a chronic multistep process over years of vaccination predisposed Ms. McCabe to rapid adverse events following Sept 11, 2010 vaccination.

Id. As with the previous eight pages of her report, Ms. Mikovits provides no support from either the literature or the record for the claims she presents.

In evaluating the contents of this report, and Ms. Mikovits' subsequent ones, the undersigned remains very concerned by Ms. Mikovits' provision of opinions outside her field of expertise. By offering diagnoses unsupported by a treating medical doctor, Ms. Mikovits not only muddies the waters by interjecting into the record statements that should not be given the weight of expert opinion, but she also undermines the credibility of all her statements. When experts are asked questions outside their area of expertise, the expert should decline to answer. If experts are willing to speak to anything, regardless of their qualifications or knowledge, it is difficult to know where the reliable testimony ends and the guesswork begins.

Respondent filed a responsive report by Dr. Whitton on October 5, 2016. Exhibit C.

2. Dr. Whitton's Background and First Report

a. Dr. Whitton's Qualifications

Dr. J. Lindsay Whitton is a research scientist specializing in immunology at the Scripps Research Institute in La Jolla, CA. He earned his undergraduate degree, medical degree, and Ph.D. from the University of Glasgow. He now serves as a professor in the Department of Immunology. While medically trained, he does not practice medicine.

b. Dr. Whitton's First Report (Exhibit C)

Dr. Whitton begins his report by rebutting Dr. Axelrod's two reports. Because, after a change in counsel, Ms. McCabe did not proceed with Dr. Axelrod's opinion, Dr. Whitton's criticisms need not be reviewed in depth. Nonetheless, it is important to note that Dr. Whitton, over the course of six pages, identified many places where Dr. Axelrod made statements that either misconstrued or had no basis at all in the literature that he had cited. See generally exhibit C at 2-7. Ms. McCabe did not obtain a response from Dr. Axelrod, leaving Dr. Whitton's critiques unrebutted. Any reliance on Dr. Axelrod's written report is, at best, questionable.

Dr. Whitton then addresses Ms. Mikovits' report, exhibit 40. Dr. Whitton begins challenging some of Ms. Mikovits' credentials. Dr. Whitton noted that Ms. Mikovits co-authored a 2009 paper that was published in the journal Science. Exhibit C at 8. This paper associated XMRV, a virus, with CFS. Id. Dr. Whitton notes that this paper has been subsequently refuted and retracted. Id. Citing her previous stance on the link between vaccination and autism, Dr. Whitton then accuses Ms. Mikovits of having an established bias against vaccinations. Id. Specifically, Dr. Whitton references Ms. Mikovits' previous claim that "a ton of data" links the two. Id. (citing Dr. Judy Mikovits Condemns Vaccines, Confirms Role in Autism, VAXXTER (Feb. 28, 2016), http://vaxxter.com/dr-judy-mikovits.[12])

Dr. Whitton addresses the substantive aspects of Dr. Mikovits' reports. Preliminarily, Dr. Whitton states confusion about the initial statements Ms. Mikovits made linking checkpoint inhibitors and Rituxan to adverse events associated with vaccines. Dr. Whitton notes that the flu vaccine is neither a checkpoint inhibitor nor a drug similar to Rituxan. Id. at 9.

Dr. Whitton then summarizes Ms. Mikovits' argument as saying that multiple influenza vaccines over the course of many years were responsible for Ms. McCabe being "always ill." Id. (referencing exhibit 40 at 4). Dr. Whitton further summarizes Ms. Mikovits' argument as postulating that the September 11, 2010 flu vaccine was the "final straw, tipping her into florid disease." Exhibit C at 9. Dr. Whitton draws on Ms. Mikovits' reference to IL-6 to infer that she believes that Ms. McCabe's IL-6 levels were chronically high, leading to her chronic illnesses. Id. Based on this understanding of Ms. Mikovits' theory of the case, Dr. Whitton then concisely states the basis for his disagreement with Ms. Mikovits' theory: "vaccine-induced cytokine responses are both limited and short-lived.

[12] Respondent did not file this article into the record.

There are no data that indicate that a vaccine can trigger long-term cytokine production in vivo." Id. at 9. He states that his opinion that cytokine responses are not known to behave in such a way is not due to a lack of research in this field but because cytokines responding in such a manner would "run contrary to everything that we know about the immune system." Id.

Dr. Whitton criticizes Ms. Mikovits for making statements regarding Ms. McCabe's diagnoses and medical care that she is not qualified to make and that are wrong. Id. First, Dr. Whitton states that, as a medically-qualified individual, he disagrees with Ms. Mikovits' statement that giving Ms. McCabe a flu vaccine was inadvisable. Id. Further, he states that Ms. Mikovits' statement that "non-infectious inflammation of the brain is the definition of encephalopathy" is "absolutely incorrect." Id. (citing exhibit 40 at 7).

Dr. Whitton then criticizes Ms. Mikovits' interpretation of the MRI Ms. McCabe received on September 24, 2010. Exhibit C at 10. He states that Ms. Mikovits is not qualified to challenge the treating physician's diagnosis and that nothing in the MRI, contrary to Ms. Mikovits' claim, links Ms. McCabe's MRI findings to the vaccine. Id.

Dr. Whitton similarly criticizes Ms. Mikovits for her diagnosis of CRS based on the symptoms that Ms. McCabe presented to Dr. Herbstein. Id. He states that her willingness to criticize the treating physicians is not appropriate given her lack of credentials, and further states that testing that Ms. Mikovits said would be definitive (i.e., tests for C-reactive protein (CRP) and erythrocyte sedimentation rates (ESR)) are non-specific and cannot provide a definitive diagnosis. Id. He further notes that Ms. McCabe actually was tested for ESR in March 2009 and that the results were normal. Id. (citing exhibit 1 at 76). Finally, Dr. Whitton criticizes Ms. Mikovits for censuring Dr. Forster for not performing tests that could have diagnosed CFS. Exhibit C at 10-11. Again, Dr. Whitton states that Ms. Mikovits is in no position to make such a criticism and that Ms. Mikovits is mistaken in saying that there exists a definitive test for CFS. Id. at 11.

In the next part of his report, Dr. Whitton states that Ms. Mikovits repeatedly conflates temporal proximity with correlation. Id. He also accuses Ms. Mikovits of overlooking relevant evidence to support a preconceived theory of vaccine causation. Id. Specifically, Dr. Whitton states that Ms. Mikovits' attempts to connect the flu vaccine to rapid brain injury, vomiting, gastric reflux, diverticulosis, and urinary tract infections are based purely on speculation because no "established scientific fact" supports a connection. Id. Further, he criticizes Ms. Mikovits for not mentioning evidence that Ms. McCabe demonstrated these

symptoms not only following administration of the vaccine, but in the months preceding the annual flu vaccinations. Id.

In the final section of his analysis, Dr. Whitton argues that Ms. Mikovits failed to provide any mechanism by which the flu vaccines could actually cause all of Ms. McCabe's symptoms. Id. at 11-12. He again states that Ms. Mikovits failed to cite any evidence that the flu vaccine could cause prolonged cytokine responses. Id. at 12. Furthermore, he questions Ms. Mikovits' basis for saying that Ms. McCabe suffered an anaphylactic reaction. Id. He notes that petitioner's other expert, Dr. Axelrod, who is actually a licensed immunologist, never referenced an anaphylactic reaction. Id. Dr. Whitton similarly questions Ms. Mikovits' assertion that molecular mimicry is involved and states that Ms. Mikovits failed to provide any mechanistic basis for a molecular mimicry explanation linking the vaccine and the injury. Id.

Dr. Whitton then identifies a number of material errors in Ms. Mikovits' report. Id. He points out that a figure cited in Ms. Mikovits report, reproduced at exhibit 40 at 4, does not actually appear in the paper she referenced. Id. at 12. He further notes that Ms. Mikovits completely misstates the contents of one of her submitted articles when she states that the article "shows recent data on lung pathology in response to flu vaccines." Id. (citing exhibit 40 at 9). Dr. Whitton points out that the article does not mention the word "lung" or "pathology." Exhibit C at 12. Finally, he notes that Ms. Mikovits' report had 12 references provided, but actually referenced only six of them in the text of the report. Id.

A status conference was held on October 21, 2016. During the status conference, the respondent requested that the petitioner again amend her petition so as to define petitioner's injury in a manner consistent with the claims made in her expert reports. Order, issued Oct. 24, 2016. Respondent also requested, again, a copy of Ms. McCabe's MRI films. Id. Finally, the parties discussed holding a hearing in late 2017. Id.

Ms. McCabe filed a status report stating that she would like to file an expert report responding to Dr. Whitton's report. Pet'r's Status Rep., filed Nov. 21, 2016. Ms. McCabe also requested until January 9, 2017, to amend her petition. Id. Ms. McCabe was given until that date to file both her amended petition and the responsive expert report. Order, issued Nov. 22, 2016.

3. Concerns Raised on December 19, 2016

The undersigned warned Ms. McCabe about deficiencies in her case in an order issued on December 19, 2016. The undersigned specifically raised the issue that Ms. Mikovits was diagnosing medical conditions when she was not qualified or licensed as a medical doctor. Order at 1. The undersigned also noted that Ms. McCabe had not produced any evidence supporting a diagnosis of a demyelinating condition and thus raised the concern that she could not proceed under the demyelination theory proffered in her petition. Id. Ms. McCabe was reminded that under Broekelschen v. Sec'y of Health & Human Servs., she must establish that she suffers from a particular injury or condition. Id. at 2 (citing 618 F.3d 1339, 1346 (Fed. Cir. 2010)). After raising these concerns, an entitlement hearing was tentatively set for October 18-20, 2017. Order at 2. Ms. McCabe was reminded to file her expert report and amended petition by January 9, 2017. Id.

C. Petitioner's Third Theory – Chronic Fatigue Syndrome

On January 9, 2017, Ms. McCabe moved for an extension of time, until March 31, 2017, to file her expert report and amended petition. While Ms. McCabe was able to file a report from Ms. Mikovits on January 9, 2017, she stated that she was unable to find a medical doctor who is an expert in ME/CFS. Exhibit 58; Pet'r's Mot., filed Jan. 9, 2017, at 1. The undersigned deferred ruling on petitioner's motion until after a status conference to be held on February 7, 2017. Order, issued Jan. 10, 2017. During the status conference, Ms. McCabe reported that she had identified a suitable expert. Order, issued Feb. 7, 2017. The undersigned then granted Ms. McCabe's motion for an extension of time to file her amended petition and expert report from a medical expert in ME/CFS, giving Ms. McCabe until April 17, 2017 to file both. Id.

1. Ms. Mikovits' Second Report (Exhibit 58)

In the first two and a half pages of Ms. Mikovits' second report, Ms. Mikovits primarily focused on rehabilitating her background. Exhibit 58 at 1-3. She notes her history of work in immune therapy in the 1980s and the contribution of her work to contemporary medicine. Id. at 2. She then details her more recent work on neuroimmune disorders. Id. She discusses her 2009 paper on the presence of XMRV in patients with ME/CFS. Id. She defends the paper, noting that the "retraction of the Science paper was political and not scientific." Id. She further notes that a 2010 paper published in the Proceedings of the National Academy of Sciences confirmed and extended the results published in the retracted 2009 article. Id. at 3 (referencing exhibit N1 (Shyh-Ching Lo et al., Detection of

MLV-related Virus Gene Sequences in Blood of Patients with Chronic Fatigue Syndrome and Healthy Blood Donors, 107 Proc. Nat'l. Acad. Sci. 15874 (2010)[13]).

Returning to the McCabe matter, Ms. Mikovits defends her use of checkpoint inhibitors and monoclonal antibody therapy as informative in a case involving an influenza vaccination. Exhibit 58 at 2. She states that the toxicities involved in these cases involve overstimulation of the same processes that are involved in a flu vaccination and thus are informative. Id.

Ms. Mikovits then restates her theory, saying that her theory was that the September 11, 2010 influenza vaccination significantly exacerbated the active preexisting inflammatory disease. Id. This worsening was through over activation and dysregulation of cytokines, chemokines, and inflammatory mediators. Id. With respect to cytokines, etc., Ms. Mikovits states: "The clinical data clearly support our theory, and that is found in the report of Dr. Axelrod, which stated that adjuvants and excipients can cause synergistic immune activation or aberrant inflammatory function of innate immune cells, including but not limited to: dendritic cells, macrophages and mast cells." Id. at 3. Although Ms. Mikovits was aware of Dr. Whitton's criticisms of Dr. Axelrod's report, Ms. Mikovits did not answer any of Dr. Whitton's criticisms. She appears to accept Dr. Axelrod's opinion without any independent analysis.

Responding to Dr. Whitton's criticism of Ms. Mikovits' willingness to make medical diagnoses and criticize the treating physicians, she states that she "did not interpret any clinical data." Id. at 4. Ms. Mikovits' statement about her lack of interpretation appears, to the undersigned, to be patently false.

Ms. Mikovits then addresses Dr. Whitton's criticism that Ms. Mikovits' theory failed to address how a flu vaccine could cause a long-term cytokine production in vivo. Id. She states that smallpox vaccination was shown to result in persistent long-term inflammation. Id.

Ms. Mikovits also notes that the ingredients in the flu vaccine "can and have been shown to contribute to systemic aberrant immune responses through overactive inflammatory mediators and persistence of dysfunctional immune cell subsets." Id. Although Ms. Mikovits uses the phrase "have been shown," Ms. Mikovits did not cite any articles where this was in fact shown.

[13] While petitioner did not file this exhibit, respondent did. This decision references respondent's exhibit.

Ms. Mikovits acknowledges that she incorrectly stated that encephalopathy was non-infectious inflammation of the brain and provided a revised definition. Id. at 5. She stated that Ms. McCabe "had many of the symptoms of myalgic encephalomyelitis within weeks of the September 11, 2012 [sic] influenza vaccination." Id. Ms. Mikovits, again, fails to identify the symptoms to which she is referring. She then states that "[Ms. McCabe] had risk factors and symptoms of both encephalitis and ME but never had a diagnosis of either. What we were actually referring to is known as secondary (post-infectious) encephalitis which is an aberrant immune system reaction that can be caused by vaccinations." Id. No support is provided for Ms. Mikovits' claim that Ms. McCabe had risk factors and symptoms of encephalitis and no reference is provided for Ms. Mikovits' claim that secondary (post-infectious) encephalitis is an aberrant immune system reaction that can be caused by vaccination. See id. at 5.

Ms. Mikovits then criticizes Dr. Whitton's assessment of the significance of the MRI results. Id. at 5. She states that several papers in the literature link influenza vaccination to a "spectrum of CNS damage including demyelination." Id. She cites "Ussel et al., Will et al., and Kim et al." Id. Ms. Mikovits did not provide any additional details (e.g., article title, journal name, publication year) about the papers named. Moreover Ms. McCabe did not enter any of these papers into the record. Thus, the accuracy of Ms. Mikovits' assertion cannot be evaluated.

Ms. McCabe filed her amended petition on April 17, 2017. On that same date she filed an expert report from her new expert, Dr. Levine. Exhibit 59.

2. Dr. Levine's Background and First Report

a. Dr. Levine's Qualifications

Dr. Susan Levine is a physician specializing in internal medicine and infectious diseases. She earned her undergraduate degree from Hunter College and medical degree from the Albert Einstein College of Medicine. She has been in private practice for 28 years. She has participated in clinical research studies looking at the mechanisms of CFS. She has served as chair of a Federal Advisory Committee on CFS.

b. Dr. Levine's First Report (Exhibit 59)

Dr. Levine begins her report by stating that Ms. McCabe had experienced "low level symptoms" of CFS following the receipt of the flu vaccine on several occasions prior to the flu vaccine in question. Exhibit 59 at 2. To demonstrate this, Dr. Levine states the following:

> On 1/6/07 following receipt of the influenza vaccine on 10/2/06 she reports symptoms of insomnia and is being treated with zolpidem, in addition to Effexor. In February of 2007 she reports wheezing and a small nodule is reported on Chest X-ray. After that, on 5/12/07, she is treated with depomedrol for a 'cough.' On 5/21/08, she is again evaluated for a 'cough.' The occurrence of allergic symptoms of which this patient's cough is a manifestation (most likely post nasal drip combined with bronchospasm) has been found to predate the actual onset of CFS. She continues to report low level symptoms of anxiety and insomnia and is once again administered a flu vaccine on 10/19/08. On 12/8/08 an endoscopy reveals 'reactive gastritis' of the antral mucosa. On 10/27/09 she reports 'gastritis' another symptom that has been found to predate the onset of CFS symptoms in a cohort of these patients.

Id.

Dr. Levine does not note that Ms. McCabe was experiencing symptoms of insomnia in the past, as established since her very first medical record filed herein. See exhibit 1 at 1. This is also true for Ms. McCabe's cough, which Ms. McCabe had since she was a child. Tr. 24. Dr. Levine also fails to mention the myriad of other symptoms that Ms. McCabe presented throughout the years covered by the records.

Dr. Levine then reviews her proposed mechanism of action linking the vaccine and Ms. McCabe's "adverse reaction". Exhibit 59 at 2-3. She states:

> Dr. Axelrod has reviewed the mechanism thought to underlie the immune response in most human subjects following the receipt of influenza vaccine. He describes the release of pro-inflammatory mediators, including IL-6 which proceed to increase permeability of the blood brain barrier and which result in the various neurological manifestations observed.

Id. at 3. Dr. Levine, like Ms. Mikovits, thus appears to adopt Dr. Axelrod's mechanism of action wholesale, with no attempt to address the numerous criticisms raised by Dr. Whitton.

Consistent with the IL-6 mediated theory adopted from Dr. Axelrod, Dr. Levine notes that IL-6 levels are elevated in senescence and that they may thus play a role in promoting aberrant responses in those at Ms. McCabe's stage of life. Id. To support this proposition, Dr. Levine cites exhibit 65 (Nathaniel D. Lambert

et al., Understanding the Immune Response to Seasonal Influenza Vaccination in Older Adults: A Systems Biology Approach, 11 Expert Review Vaccines 985 (2012)).

Dr. Levine then proposes a "kindling" model for the etiology of Ms. McCabe's CFS. Exhibit 59 at 3. She states that this theory proposes that repeated exposure to an initially sub-threshold stimulus can eventually result in a suprathreshold response, manifesting as "spontaneous seizure like activity." Id. Why Dr. Levine references "seizure like activity" is not readily apparent since seizures do not appear in the record.

Dr. Levine proceeds to state that infectious agents (both live viruses and vaccines) can "influence secretion of Adrenocorticotropic hormone (ACTH) in the brain." Id. Dr. Levine does not provide support for this proposition, however. She continues to state that this can ultimately lead to "lowered plasma levels of cortisol" which accounts for the fatigue, insomnia, and adverse response to stress seen in CFS patients. Id. For this line of logic, Dr. Levine cites exhibit 66 (Leonard A. Jason et al., An Etiological Model for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, 2 Neuroscience and Medicine 14 (2011)).

Dr. Levine proceeds by noting that "immunization of humans with vaccines of many types, including MMR, pneumovax, hepatitis B, tetanus, typhoid and polio, as well as anthrax have been implicated in the development of CFS." Exhibit 59 at 3. In support of this proposition, Dr. Levine cites exhibit 68 (L.D. Devanur & J.R. Kerr, Chronic Fatigue Syndrome, 37 J. Clinical Virology 139 (2006)).

To further support the link between vaccines and CFS, Dr. Levine cites an article presenting a case study of a young woman who developed POTS with chronic fatigue two months following her vaccination with human papillomavirus vaccine. Exhibit 59 at 3 (citing exhibit 69 (Lucija Tomljenovic et al., Postural Orthostatic Tachycardia With Chronic Fatigue After HPV Vaccination as Part of the "Autoimmune/Auto-inflammatory Syndrome Induced by Adjuvants", 2 J. Investigative Medicine High Impact Case Reports 2324709614527812 (2014)). In a similar vein, she states that there has been a link between the Pandemrix flu vaccine and narcolepsy. Exhibit 59 at 4. She cites two articles in support of this proposition: exhibit 70 (A. Nellore & T. Randall, Narcolepsy and Influenza Vaccination-The Inappropriate Awakening of Immunity, 4 Annual Translational Medicine S29 (2016)) and exhibit 71 (A. Sohail Ahmed & Lawrence Steinman, Narcolepsy and Influenza Vaccination-induced Autoimmunity, 5 Annual

Translational Medicine 25 (2017)). Dr. Levine refers to the case of Pandemrix as a "related clinical model of neurological dysfunction" that is a "plausible mechanism to explain the course of this patient's illness." Exhibit 59 at 4.

Dr. Levine summarizes her opinion: that Ms. McCabe's "repeated exposures" to the flu vaccine in conjunction with her premorbid symptoms (gastrointestinal, allergic, and neuropsychological) facilitated the 2010 flu vaccine "catapult[ing]" her into a diagnosis of CFS. Id.

3. Concerns Raised on April 20, 2017.

The undersigned reviewed Dr. Levine's report in conjunction with the newly filed petition and identified numerous issues in the report that Ms. McCabe would need to address. See order, issued April 20, 2017. For one, Dr. Levine failed to state the diagnostic criteria she was using to diagnose Ms. McCabe with CFS and what the basis in the record was for this diagnosis. Id. at 1. In addition, Dr. Levine failed to provide adequate support for the following five items in her report: 1) The link between IL-6 and CFS and why IL-6 is important in this case; 2) The basis for her "kindling" theory; 3) The link between ACTH and the influenza vaccine, and its importance to this case; 4) The link between oxidative stress, the flu vaccine, and CFS, and its importance to this case; and 5) The importance of the HPV-POTS case study she cites to Ms. McCabe's case. Id. at 1-2. The undersigned also stated that Dr. Levine's report failed to provide any opinion regarding the appropriate timing between the flu vaccine and the onset of Ms. McCabe's putative CFS. Id. at 2-3.

With regard to the amended petition, the undersigned sought to confirm that Ms. McCabe was not proceeding with either the theory that the flu vaccine caused her to develop or significantly aggravate a demyelinating condition (as Dr. Axelrod suggested) or the theory that the flu vaccine caused cytokine release syndrome (as Ms. Mikovits suggested). Id. at 3. Ms. McCabe was given until May 12, 2017 to file a supplemental report from Dr. Levine. Id. at 4. Ms. McCabe timely filed the supplemental report on May 12, 2017. Exhibit 72.

4. Dr. Levine's Supplement to her First Report (Exhibit 72)

Dr. Levine attempts to address the concerns raised in the April 20, 2017 order. With respect to the diagnosis of CFS, Dr. Levine cites a number of Ms. McCabe's symptoms in the years prior to and following the 2010 vaccination and then concludes that "the complaints reported by the patient in the above Exhibits match the symptoms and exclusionary criteria contained in the case definitions provided in References 1 and 2." Exhibit 72 at 1-2. References 1 and 2 are exhibit

61 (Leonard A. Jason et al., Data Mining: Comparing the Empiric CFS to the Canadian ME/CFS Case Definition, 68 J. Clinical Psychology 41 (2012)) and exhibit 62 (B.M. Carruthers et al., Myalgic Encephalomyelitis: International Consensus Criteria, 270 J. Internal Medicine 327 (2011)).

Dr. Levine then expands on her claim that the influenza vaccination can result in the "release of a major pro-inflammatory cytokine, IL-6." Exhibit 72 at 2. She states that a number of links between IL-6 and actual influenza viral infection are "well established" and states that the same is "presumably" true for influenza vaccine. Id. However, she provides no basis for why a live infection would cause the same response as the response to an inert substance. She further notes that mice lacking IL-6 are not able to respond to viral infections properly. Id. at 2-3 citing exhibit 73 (Sarah N. Lauder et al., Interleukin-6 Limits Influenza-induced Inflammation and Protects Against Fatal Lung Pathology, 43 European J. Immunology 2613 (2014)).

Dr. Levine continues, noting that poor sleep quality is associated with elevated levels of IL-6. Id. at 3. She concludes that this association indicates that there is a "common pathophysiological mechanism between influenza vaccination and the pathogenesis of ME/CFS." The undersigned does not understand how this premise links to the conclusion she draws. For example, poor sleep quality may cause an increase in IL-6 or both may be affected by some other biologic process.

To lend additional support to her claim that IL-6 as well as other pro-inflammatory cytokines have also been implicated in the pathophysiology of ME/CFS, Dr. Levine cites exhibit 75 (L. Russell et al., Illness Progression In Chronic Fatigue Syndrome: A Shifting Immune Baseline, 17 BMC Immunology 3 (2016)). Exhibit 72 at 3. She similarly cites to exhibit 76 (Hyong Jin Cho et al., Association Of C-Reactive Protein And Interleukin-6 With New-Onset Fatigue In The Whitehall II Prospective Cohort Study, 43 Psychological Medicine 1 (2013)) to show that "along with C reactive protein, plasma levels of IL-6 were found elevated in a large scale cohort study that correlated with occurrence of systemic inflammation with the onset of fatigue." Exhibit 72 at 3. Dr. Levine concludes her discussion of the link between IL-6 and CFS by noting that the measurement of cytokines such as IL-6 is not yet used in clinical settings and that it is not unusual that Ms. McCabe did not undergo a test for cytokine levels. Id.

Dr. Levine next expands on her "kindling" model of CFS. Id. at 3-4. In further describing the model, Dr. Levine states that it is a "likely model" for the pathophysiology of ME/CFS and said it occurs when a subject has repeated exposure to a subthreshold stimulus. Id. at 3. She states that repeated vaccine

administration and co-incident low-level symptoms constituted such a subthreshold stimulus in Ms. McCabe's case. Id.

To support this theory, Dr. Levine again cites exhibit 61 (Jason). She stated that the model puts forth how an "infectious agent like the influenza vaccine" can affect cortisol secretion. Exhibit 72 at 4 (citing exhibit 61 (Jason)). This, she argues, can also result in oxidative stress, leading to cognitive dysfunction. Exhibit 72 at 4. Dr. Levine summarizes her kindling model in the case of Ms. McCabe:

> Therefore, this theory of 'kindling' . . . describes the evolution of this patient's symptoms over time as outlined in part by the exhibits above listing all the symptoms that have been found in studies to PREDATE the onset of actual ME/CFS, such as insomnia, allergies and gastritis, until her last influenza vaccine which 'acts to break the camel's back' so to speak and thrusts Ms. McCabe into full blown ME/CFS.

Id.

As evidence of Ms. McCabe's neurological dysfunction, Dr. Levine references Dr. Herbstein's recital of Ms. McCabe's symptoms. Id. Dr. Levine's reliance on Dr. Herbstein is strange since Dr. Herbstein concluded, after actually examining her, that Ms. McCabe was neurologically normal. See exhibit 6 at 4 ("The patient presents with multiple symptoms and basically a normal neurological exam").

Dr. Levine then puts forth exhibit 78 (Ian Hickie et al., Post-Infective and Chronic Fatigue Syndromes Precipitated by Viral and Non-Viral Pathogens: Prospective Cohort Study, 333 BMJ 575 (2006)). Exhibit 72 at 4-5. She states that this article "demonstrates that irrespective of the infectious agent that 'triggers' the onset of the symptoms of CFS, there is a reproducible pattern of illness that occurs in certain susceptible individuals following exposure to such an agent." Id. She concludes this line of reasoning by stating that "[t]herefore, HPV and influenza vaccine can both trigger the symptom complex of ME/CFS in a vulnerable subject." Id. at 5. Thus, to Dr. Levine, the case reports linking HPV vaccine with POTS are relevant to a theory that flu vaccine can cause CFS. Dr. Levine asserts that "because vaccines induce an immune response similar to infections, they may also, just like infections, trigger autoimmune diseases." Exhibit 72 at 4. Dr. Levine concludes her second report by stating that "two different theories are plausible in linking the administration of flu vaccine in this patient and the subsequent onset of ME/CFS." Id. Unfortunately, her report is not clear about what these two theories are. She subsequently restates the kindling theory, identifying some of Ms. McCabe's medical history and previous flu

vaccinations and how these constitute "subliminal" symptoms over a four-year period. Id. However, her second theory appears to be left unstated.

5. Concerns Raised on May 30, 2017

A status conference was held on May 30, 2017, to discuss Dr. Levine's supplemental report. The undersigned noted that Dr. Levine again failed to identify the appropriate timing for each of her theories linking the vaccine with Ms. McCabe's putative CFS. Order, issued June 1, 2017, at 1. Further, Dr. Levine failed to define what symptoms she attributes to Ms. McCabe's putative CFS. Id. Petitioner requested an opportunity to file a supplemental report from Dr. Levine and the undersigned granted that opportunity. Id. at 1-2. The Secretary was also ordered to file his responsive reports. Id. at 2. The Secretary noted that he would be filing a responsive report from Dr. Whitton, and would also be retaining a rheumatologist to provide an opinion. Id. The Secretary filed Dr. Whitton's responsive report on June 27, 2017. Exhibit F.

6. Dr. Whitton's Responsive Report (Exhibit F)

Dr. Whitton's second report addressed Ms. Mikovits' report, exhibit 58. Generally, Dr. Whitton states that Ms. Mikovits' second report does not "present any new, or logical, explanation for why [Ms. Mikovits and Mr. Ruscetti] believe that the vaccine administered to Ms. McCabe on 9/11/2010 caused harm." Exhibit F at 1. Dr. Whitton further states that the second report, like her first, contains incomplete and incorrect citations while omitting reference to some of the cited papers. Id.

Dr. Whitton begins his rebuttal by pointing out that Ms. Mikovits failed to address his point that in the six years since the vaccine, Ms. McCabe has never been diagnosed with a demyelinating disease. Id. This leads Dr. Whitton to point out that it is impossible for the vaccine to have caused or aggravated a condition that Ms. McCabe does not appear to have. Id.

Dr. Whitton then comments on Ms. Mikovits' defense of her retracted 2009 article. To summarize the previous discussion, Ms. Mikovits claimed that her article was retracted for political as opposed to scientific purposes. Exhibit 58 at 2. As support for this claim, Ms. Mikovits stated that a 2010 article published in the Proceedings of the National Academy of Sciences confirmed the 2009 article's findings. Id. (citing exhibit N1 (Lo et al. (2010))). Dr. Whitton states that this 2010 article was also retracted. Exhibit F at 2. The undersigned agrees with Dr. Whitton that Ms. Mikovits' citation to two retracted articles without noting either retraction diminishes her credibility.

Dr. Whitton then rebuts Ms. Mikovits' reference to the smallpox vaccine as being an example of how a vaccine can result in a prolonged cytokine response. Exhibit F at 2-3. Dr. Whitton does not disagree that there is a prolonged response to the smallpox vaccine. Id. at 3. Instead, he points out that the smallpox vaccine that Ms. Mikovits was referencing was a live-virus vaccine that "replicates quite well and often causes the formation of a pock that takes some time (7-10 days) to resolve." Id. In contrast, he notes, the viral components that make up the influenza vaccine in question are killed and do not replicate, resulting in "less marked innate and adaptive immune responses." Id. In conclusion, Dr. Whitton states that Ms. Mikovits' most recent report does not alter his opinion that there is no evidence to support the conclusion that the flu vaccine can cause, in vivo, anything more than a "limited and short-lived" cytokine response. Id. at 4-5.

On June 30, 2017, petitioner moved for a two-week extension of time to file her supplemental report from Dr. Levine. Petitioner's motion was granted. Order, issued July 10, 2017. Ms. McCabe timely filed Dr. Levine's supplemental report on July 14, 2017. Exhibit 80.

7. Dr. Levine's Second Supplemental Report (Exhibit 80)

As discussed above, Dr. Levine's supplemental report was supposed to respond to the undersigned's request for clarification on the mechanism Dr. Levine was proposing to connect the flu vaccine and CFS. Order, issued June 1, 2017. Dr. Levine was also instructed to opine on the appropriate timing of this proposed mechanism. Id. Dr. Levine was also ordered to file a clear statement about which medical records Dr. Levine associated with CFS. Id.

Unfortunately, Dr. Levine's new report provides little new information. She states that following her October 2, 2006 flu vaccine, "Ms. McCabe complained of worse insomnia, a key symptom of ME/CFS, 3 months later." Exhibit 80 at 1. Dr. Levine also notes Ms. McCabe's diagnosis of gastritis two months after her October 2008 vaccination, which Dr. Levine says is "a notable symptom found in ME/CFS patients." Id. Dr. Levine states that these events were kindling to her "full blown" ME/CFS three days following her September 2010 flu shot. Id. at 2. Dr. Levine associates this "full blown" ME/CFS with her cognitive complaints noted on September 14, 2010 as well as the MRI of her brain that noted demyelinating lesions, which Dr. Levine stated are thought to be autoimmune in nature. Id. at 1-2.

Dr. Levine asserts that her references to IL-6 are based on research studies of ME/CFS, although she does not cite any studies. Id. at 1. She states that we do not know about Ms. McCabe's IL-6 levels because the physicians treating Ms.

McCabe did not realize at the time that she was suffering from ME/CFS. Id. Dr. Levine revisits the case report of a girl who developed POTS after a HPV vaccination. Id. at 2. Dr. Levine notes that the girl had elevated antinuclear antibody (ANA) levels two months after receipt of the HPV vaccination. Id. Dr. Levine states that "we can assume [that the HPV vaccination] can cause an adverse reaction similar to that of the influenza vaccine." Id. Beyond a temporal sequence of events, there does not appear to be support for the claim presented here that the HPV vaccination caused the elevated levels of ANA.

Dr. Levine concluded her report by stating:

> Finally, the occurrence of symptoms associated with ME/CFS within months of Ms. McCabe's receipt over a five year period, initially controllable with medication established a pattern of symptoms outlined in reference 6, which describes 'kindling'. This is a term that explains the occurrence of some symptoms, such as insomnia or migraine headaches or allergies in future ME/CFS patients and which may act as a harbinger for full blown disease. Ms. McCabe developed symptoms of insomnia treated with zolpidem on 1/6/07 after receipt of influenza vaccine on 10/2/06 but was able to continue working.
>
> Three days after receipt of influenza vaccine on 9/11/10 she developed full blown ME/CFS with symptoms of confusion and significant cognitive dysfunction which completely interfered with her life. The timing of the onset of her symptoms after vaccinations in this case is completely appropriate.

Id.

8. Concerns Raised on August 1, 2017

After reviewing Dr. Levine's most recent submission (exhibit 80), the undersigned issued an order on August 1, 2017, stating that the hearing may not be able to proceed as scheduled due to problems with the reports. See order at 1. The order reviewed the background of the current issue: A December 19, 2016 order highlighted major issues with petitioner's case and directed petitioner to clarify Ms. McCabe's specific injury and how that injury was linked to the flu vaccine she received. Id. at 1. Despite over seven months' time since that order, petitioner had still failed to present a cogent expert report. The most recent report from Dr. Levine, the undersigned noted, failed to explain her conclusion that the temporal relationship between the flu vaccine and petitioner's symptoms was appropriate. Id. at 2.

Furthermore, based on Dr. Levine's most recent reports, the undersigned noted that it appeared that petitioner was pivoting toward a claim of significant aggravation without providing any evidence demonstrating significant aggravation compared to a normal progression of CFS. Id. at 3. In conclusion, the undersigned noted: "[i]n short, from a review of the reports from the petitioner's experts, it appears that petitioner's case may not be complete and may not be coherent. Petitioner may, with additional work and additional disclosures, put together a persuasive case. That development should take place before the hearing." Id. The order scheduled a status conference on August 17, 2017, to discuss how the petitioner would like to proceed. Id.

Prior to, and in the days immediately following, the status conference, respondent filed responsive reports from Dr. Whitton (exhibit G), Dr. Leist (exhibit J), and a new expert, Dr. Matloubian (exhibit H).

9. Dr. Whitton's Third Report (Exhibit G)

Dr. Whitton's third report responds to Dr. Levine's first three reports (exhibits 59, 72, and 80).

Dr. Whitton began by criticizing Dr. Levine for adopting Dr. Axelrod's assertion that the influenza vaccine could result in sustained production of IL-6, resulting in the degradation of the blood brain barrier. Exhibit G at 3. Dr. Whitton states that this unsupported assumption underlies Dr. Levine's theory and incorporates his previous rebuttal to this assertion. Id.

Dr. Whitton then addresses Dr. Levine's kindling theory, linking subthreshold neurological insults to the development of ME/CFS. Dr. Whitton states that he is aware of the kindling theory in relation to seizure disorders. Id. However, he states that he is not aware of any evidence that supports the concept of kindling in the realm of immunology and ME/CFS specifically. Id. He further states that Dr. Levine's report provides no such evidence. Id.

Dr. Whitton next evaluates exhibit 68 (Devanur), which was cited by Dr. Levine to support her claim that vaccines have been shown to cause CFS. Exhibit 59 at 3. He states that Dr. Levine mischaracterized what the article was reporting. According to Dr. Whitton, the article was not itself saying that vaccines have been shown to cause CFS, but that, and he quotes the article, "immunization with various vaccines have been *reported* to trigger CFS." Id. at 3-4 (quoting exhibit 68 (Devanur) at 7). He further notes that the Devanur article based this association on case reports only, not on experimental studies demonstrating causation. Exhibit G

at 3-4. Thus, to cite exhibit 68 (Devanur) as evidence of causation would be vastly overstating the strength of the evidence. Id.

Following up on the evidence linking the influenza vaccine with CFS, Dr. Whitton introduces exhibit G2 (Per Magnus et al., Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME) Is Associated With Pandemic Influenza Infection, But Not With An Adjuvanted Pandemic Influenza Vaccine, 33 Vaccine 6173 (2015)). This epidemiological study followed the population of Norway during the H1N1 pandemic and measured onset of CFS in patients who were either vaccinated with the H1N1 vaccine (Pandemrix) or who (likely) were infected with the H1N1 virus.[14] Vaccination, infection, and diagnosis of CFS was determined through the Norwegian immunization registry, reimbursement data from primary care physicians, the Norwegian surveillance system for communicable diseases, and the national specialists health care register. The study's authors tracked individuals from the onset of the peak of the H1N1 pandemic (October 1, 2009) through either their emigration, death, or the end of the study (December 2012) and examined the relative hazard ratio (HR) of vaccination, infection, and their interaction. The major results are reproduced in the table below:

Table 3
Incidence rates and hazards ratios (HRs) of CFS/ME, with associated 95% confidence intervals (CIs), according to exposure to pandemic vaccination and influenza infection. Follow-up time from October 1, 2009, through December 31, 2012, for 4822,377 residents of Norway born 1899–2009.

		No. of person-months at risk	No. of cases	Incidence rate*	Adjusted**	
Vaccinated	Infected				HR	95% CI
No	No	107,475,182	2165	2.01	1.0	
Yes	No	67,985,240	1345	1.98	0.98	0.91–1.05
No	Yes	3032,843	164	5.41	2.08	1.78–2.44
Yes	Yes	1,389,917	63	4.53	1.88	1.46–2.42

* Number of new cases per 100,000 person-months at risk.
** Stratified Cox analysis with separate baseline hazards functions for each year-of-birth category and adjusted for sex.

As the table indicates, infection with the H1N1 virus was associated with a twofold increase in the relative risk of subjects being diagnosed with CFS. However, vaccination itself was not associated with any change in the relative risk of subjects being diagnosed with CFS. As the authors conclude: "This suggests that development of CFS/ME may be a reaction to fever, malaise, and general activation of the immune system, rather than the more restricted antigenic stimulation from a vaccine." Id. at 6175.

Dr. Whitton then comments on Dr. Levine's second report (exhibit 72). Dr. Whitton points out that Dr. Levine's discussion of IL-6 fails to address how the flu

[14] The authors presumed that a diagnosis of a "flu-like" illness during the peak pandemic period reflected a H1N1 infection, but excluded all diagnoses of "flu-like" illness outside of the peak pandemic period. When antigenic testing was used to diagnose H1N1, the authors did not exclude cases based on when the diagnosis occurred.

vaccine can trigger a large and/or long-term increase in IL-6 levels. Exhibit G at 4. This criticism relates back to Dr. Whitton's comments on Dr. Axelrod's theory and his criticism that Dr. Levine adopted this theory without independent examination. Id.

Regarding the kindling theory, Dr. Whitton states that the kindling theory is only an untested model that "may have value in relation to the [central nervous system]," since that is the system in which it has been shown, but that in the realm of immunology it "barely reaches the level of a hypothesis." Exhibit G at 4-5.

Dr. Whitton then addresses the "seminal" paper that Dr. Levine put forth as linking the flu vaccine and Ms. McCabe's CFS. This article was entered as exhibit 78 (Hickie). To recap, Dr. Levine had stated that the article stood for the conclusion that "HPV and influenza vaccine can both trigger the symptom complex of ME/CFS." Exhibit 72 at 5. Dr. Whitton states that he carefully read the paper and notes "the word vaccine (nor any relative thereof) does not even appear in the main text." Exhibit G at 5.

Dr. Whitton's assessment of the conclusion of Dr. Levine's second report was similar to the undersigned's insomuch as he is also unable to discern what are the "two different theories" that Dr. Levine says can account for linking Ms. McCabe's flu vaccine with her CFS. Id. (commenting on exhibit 72 at 5).

Finally, Dr. Whitton comments on Dr. Levine's third report (exhibit 80). Exhibit G at 5-6. The issues Dr. Whitton claims with regard to Dr. Levine's third report parallel the issues he raised with regard to reports one and two. Dr. Whitton states that Dr. Levine did not provide any additional insight on how a flu vaccine can cause insomnia three months after one administration of flu vaccine and can cause gastritis two months after another administration. In addition to the lack of foundation for a claim of causation, Dr. Whitton notes that Ms. McCabe was experiencing insomnia at the time of the first submitted medical record from October 2006. Id. at 6 (citing exhibit 1 at 3).

10. Dr. Matloubian's Background and First Report

a. Dr. Matloubian's Qualifications

Dr. Mehrdad Matloubian is a physician-scientist specializing in rheumatology and internal medicine at the University of California San Francisco. He earned his undergraduate degree, M.D., and Ph.D. from the University of California Los Angeles. He now serves as an Associate Adjunct Professor with the University of California San Francisco.

b. Dr. Matloubian's First Report (Exhibit H)

Dr. Matloubian begins by reviewing Dr. Levine's reports. See exhibit H at 2. He stated that Dr. Levine failed to provide any evidence that the influenza vaccine leads to persistent elevation of IL-6, or any other cytokine following immunization. Id. He also stated that Dr. Levine consistently treated an influenza infection and the influenza vaccine as being somehow equivalent. Id. Dr. Matloubian states that this is "not scientifically correct." Id. Finally, he noted that while some evidence shows that CFS may follow an infection, CFS is not associated with flu infection, much less a flu vaccine. Id.

Dr. Matloubian then presents the 2015 Institute of Medicine (IOM) report on CFS. Exhibit M1 (IOM, Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness, Nat'l Acad. Press (2015)). Dr. Matloubian summarizes the IOM's major findings and recommendations, beginning with its proposed diagnostic criteria. See exhibit H at 2-4.

For diagnosis of CFS, the IOM committee recognized that there does not exist "objective abnormal findings either clinically or through the use of diagnostic tools that are readily available" and that "the diagnosis depends solely on patient reported symptoms after other possibilities have been excluded." Exhibit H at 2. According to Dr. Matloubian, the IOM committee's criteria for ME/CFS requires the presence of at least three symptoms: profound fatigue not relieved by rest, post-exertional malaise, and unrefreshing sleep. Exhibit H at 2 (citing exhibit M1 (IOM) at 210). The diagnosis further requires either cognitive impairment or orthostatic intolerance. Id. Dr. Matloubian concludes that Ms. McCabe's symptoms do not support the diagnosis of ME/CFS based on the above criteria for the following reasons: 1) sleep apnea was never addressed as the cause of Ms. McCabe's sleep disturbances and chronic fatigue, and 2) Ms. McCabe had no neurological impairments or orthostatic intolerance. Id. at 2-3.

For the etiology of ME/CFS, Dr. Matloubian then reviews what the IOM said is known about the etiology of ME/CFS. Id. at 3. In short, he states that "all experts agree that the cause is unknown." Id. He does note that the IOM panel states that there is "high quality" data linking the involvement of the immune system. Id. (citing exhibit M1 (IOM) at 152). However, it is not clear from this data whether the immune system changes associated with CFS are a cause or effect of the disease. Id. Furthermore, while the committee did resolve that some parts of the immune system are known to be dysregulated in CFS patients (e.g., natural killer cells), it was not able to reach a definite conclusion regarding cytokine abnormalities and CFS. Id. As with natural killer cells, it is not known if any cytokine imbalances (to the extent they exist) are a cause or effect of ME/CFS. Id.

Whether there exists a causal link between IL-6, or any other compound, and CFS appears to be secondary—in this case, at least—to the question of whether the flu vaccine is associated with dysregulation of these compounds. That is the next question that Dr. Matloubian addresses. To begin, Dr. Matloubian reviews the mechanisms of influenza infections and contrasts this process with what occurs when one receives a flu vaccination. Exhibit H at 4. As reported in the manufacturer's statement, the virus is fixed and killed with formaldehyde and then broken down using a detergent. Id. at 5. The result is a compound that is incapable of replication. Id. He further notes that Ms. McCabe's September 2010 flu vaccine, Fluzone, did not contain any adjuvants. Id. at 6. Because of the characteristics of the killed and broken down vaccine, the remaining proteins do not "present as a threat to the individual as does the influenza virus, and hence, do[] not require the same host defense pathways and cytokines for protection." Id.

Thus, Dr. Matloubian concludes, the pertinent question for this case under petitioner's theory is whether the flu vaccine (and not the flu virus) can cause sustained production of cytokines such as IL-6. Id. He puts forth exhibit M5 (J.P. Valensi et al., Systemic Cytokine Profiles In BALB/C Mice Immunized With Trivalent Influenza Vaccine Containing MF59 Oil Emulsion And Other Advanced Adjuvants, 153 J. Immunology 4029 (1994)). Referencing this article, Dr. Matloubian states that the authors measured several cytokines in mice serum starting three hours after vaccination with an inactivated virus. The study was done with and without the presence of adjuvants. The results, he states, are that detectable levels of IL-6 were not found even up to 24 hours after vaccination when the vaccine was not supplemented with an adjuvant. Exhibit H at 6.

Dr. Matloubian also offers exhibit M6 (J.U. McDonald et al., Inflammatory Responses to Influenza Vaccination at the Extremes of Age, 151 Immunology 451 (2017)). This article, Dr. Matloubian states, examined both young and old mice's

cytokine levels in response to an inactivated influenza vaccine. Exhibit H at 6. Dr. Matloubian states that the authors found that any cytokine induction was "transient" and the levels "returned to baseline values usually within 24 hours after immunization." Id.

The studies referenced in exhibits M5 and M6 were both done on mice. Dr. Matloubian also offers exhibit M7 (J.C. Eriksson et al., Local and Systemic Cytokine and Chemokine Responses after Parenteral Influenza Vaccination, 1 Influenza and Other Respiratory Viruses 139 (2007)). In this article, Dr. Matloubian states that the authors did not find significant elevation of inflammatory cytokines in the sera of immunized human subjects one and two weeks after immunization. Exhibit H at 6.

Dr. Matloubian concludes on the basis of these studies that "it is not clear how in a biologically plausible manner [a flu vaccine] could lead to sustained levels of IL-6." Id. Because Dr. Levine, Ms. Mikovits, and Dr. Axelrod used IL-6 to connect the vaccine to the putative ME/CFS, it is thus not clear, according to Dr. Matloubian, how the vaccine and the ME/CFS can be connected. Id.

Dr. Matloubian acknowledges that while ME/CFS has been associated with certain viral infections, influenza virus is not on the "usual list of culprits." Id. at 7. He cites exhibit M1 (IOM) at 157-62 and exhibit 78 to support this proposition. Id. According to Dr. Matloubian, the viruses associated with ME/CFS are usually those that have large genomes with complex replication cycles that result in a chronic latent infection. Exhibit H at 7-8. Infections with these viruses can result in a chronic stimulation of the immune system, driving inflammation. Id. at 8. In contrast, the flu virus is a small genome virus that does not result in a chronic or latent infection. Id. at 8. Therefore, the virus is much less likely to be a cause of ME/CFS.[15] Id.

Dr. Matloubian then addresses, in great detail, some of the statements made by Dr. Levine connecting vaccines to autoimmune disorders. First, he addresses her point that previous associations between the Pandemrix vaccine and narcolepsy support her argument connecting the Fluzone vaccine with ME/CFS. Id. Dr. Matloubian rebuts this by saying that the mechanism thought to associate autoimmunity and narcolepsy—the HLA DQB1*0602 haplotype—is not present in

[15] While influenza may be much less likely to cause CFS compared to other infections, in at least one epidemiological study, exhibit G2 (Magnus), influenza infection (but not vaccination) was associated with a two-fold increase in the relative risk of a person being diagnosed with CFS. See Section II.C.9, above.

the case of ME/CFS. Id. Second, unlike CFS, narcolepsy has been associated with infections with the H1N1 virus.[16] Id. Third, the cases showing a connection between the flu vaccine and narcolepsy occurred with only one specific vaccine preparation, which was adjuvanted. Id. It has not been associated with other preparations of the flu vaccine. Id. Further, Dr. Matloubian notes that the connection between the Pandemrix preparation and narcolepsy is, itself, still a matter of debate. Id.

Dr. Matloubian then addresses the connection that Dr. Levine raised between the HPV vaccine and POTS. Id. at 8-9. He notes that the woman in question may have had a pre-existing autoimmune disease, such as lupus. Id. at 9. He further states that this case study was merely a case study, and provided no empirical basis for concluding a causal connection exists. Id. Furthermore, the mechanism proposed in the case study is not applicable to Ms. McCabe's case since the HPV vaccine is adjuvanted, unlike the flu vaccine in question here. Id. Finally, he asserts that the difference in the genetic makeup between HPV and flu virus makes a hypothetical mechanism based on molecular mimicry "extremely unlikely." Id.

In the last portion of his opinion addressing Dr. Levine's medical theory, Dr. Matloubian speaks to Dr. Levine's assertion that "aberrant ACTH secretion explains in part the mechanism by which the HPA axis can enhance the effect of an 'infectious agent' like the influenza vaccine by lowering cortisol levels (via the HPA axis) and heightening the pro-inflammatory response." Exhibit H at 9 (citing exhibit 72 at 4). Dr. Matloubian, again, notes that inactivated flu vaccine is not an infectious agent and that to label it as one is not correct. Exhibit H at 9. He further comments that the IOM committee found that there was insufficient evidence to conclude that any specific neuroendocrine abnormalities cause ME/CFS. Id. (citing exhibit M1 (IOM) at 157).

Dr. Matloubian next addresses the issue of timing. He states that based on animal models with non-adjuvanted influenza vaccines, there are no measureable systemic levels of IL-6 at 3, 6, 12, and 24 hours after immunization. Exhibit H at 9. In addition to the time it takes to produce the cytokines, he noted there is the delay between their production and any effect they may have on the subject's nervous system function. Id. at 9-10. He comments that this timeline is inconsistent with petitioner's claim that the symptoms began 6 hours after her immunization. Id. at 10. Finally, he returns to his earlier observation that cytokine

[16] But see footnote 11 and Section II.C.9, above (at least one epidemiological study has associated CFS with influenza, but not influenza vaccine).

responses are "quite low in magnitude and short-lived" and thus would not explain symptoms that occurred weeks to months later. Id.

11. Dr. Leist's Supplemental Report (Exhibit J)

Dr. Leist submitted a brief supplemental report on August 23, 2017, which provided an analysis of the MRI performed on Ms. McCabe on September 24, 2010. Exhibit J. Dr. Leist said that he concurs with the radiologists' assessment that the three subcortical white matter hyperintensities were not specific for any particular pathobiology. Id. at 1. Furthermore, he associates the hyperintensities with Ms. McCabe's history of cardiovascular disease (including chest pain, palpitations, tachycardia, and COPD). Id. To support his assertion that these cardiovascular conditions are "known to be associated" with cerebral white matter changes, Dr. Leist cites one article. Exhibit J at 1 (citing exhibit J2 (C.A. Spilling et al., White Matter Lesions Characterize Brain Involvement In Moderate To Severe Chronic Obstructive Pulmonary Disease, But Cerebral Atrophy Does Not, 17 BMC Pulmonary Medicine 92 (2017))).

12. Concerns Raised in August 2017 Status Conferences

During an August 17, 2017 status conference, petitioner's attorney stated that he was not familiar with the contents of the August 1, 2017 order. Order, issued Aug. 17, 2017, at 1. He attributed his lack of preparedness to an unexpected family development. Id. The undersigned conveyed to the petitioner that between the issues presented in the August 1, 2017 order and the issues identified by Dr. Whitton's and Dr. Matloubian's more recently filed expert reports, there was a concern that a reasonable basis for proceeding to the hearing did not exist. Id. A status conference was set for August 30, 2017, to further discuss the issues. Id.

During the August 30, 2017 status conference, petitioner stated that she intended to proceed with the hearing. Order, issued Aug. 31, 2017, at 1. The Secretary argued that a hearing was not appropriate because petitioner had failed to present evidence regarding the appropriate timing for the link between the vaccination and CFS. Id. In addition, the Secretary argued that no evidence of significant aggravation had been presented. Id. The undersigned stated his concern that there were significant gaps in petitioner's case and urged Ms. McCabe to address these gaps in her pre-trial brief and final expert statements. Id. at 1-2.

13. Ms. Mikovits' Final Report (Exhibit 81)

Ms. Mikovits submitted a final report on September 5, 2017. Exhibit 81.

In this report Ms. Mikovits states that the status of Ms. McCabe's health, particularly with respect to the worsening inflammatory gastrointestinal disease she suffered in the year prior to the vaccination, resulted in a critical and profound disruption of the gut microbiota. Id. at 2. The September 11, 2010 vaccination, because it was given prior to the resolution of this condition, resulted in the immediate development of severe and life-changing ME/CFS from which she has not recovered. Id.

Ms. Mikovits comments that at the time of her 2010 vaccination, Ms. McCabe had been diagnosed with sinusitis, bronchitis, severe gastritis, COPD, asthma, IBS, diverticulitis, and depression. Id. Ms. Mikovits asserts that these are "all inflammatory diseases" that are "caused in part by dysregulation of inflammatory cytokines and chemokines." Id.

Regarding her diagnosis, Ms. Mikovits notes that at the time of the September 11, 2010 vaccination, the International Consensus diagnostic criteria for ME/CFS had not yet been published. Id. She then states that the "most rigorous" criteria at the time was the Canadian Consensus Criteria (CCC). Id. Ms. Mikovits states that the CCC does not provide for a diagnosis of ME/CFS if the patient has received any other diagnosis for the symptoms. Id. In other words, it was strictly a diagnosis of exclusion. Therefore, because Ms. McCabe had been diagnosed with another disorder that could account for her symptoms (e.g., depression, insomnia), she was precluded from a ME/CFS diagnosis at that time. Id. Ms. Mikovits concluded that "under today's definition, [Ms. McCabe] would have received a diagnosis of ME/CFS." Id. at 2. It is notable, given Ms. Mikovits' proclamations to the contrary, that no treating physician has ever diagnosed Ms. McCabe with CFS. Ms. Mikovits again appears to be playing (medical) doctor.

Ms. Mikovits states that Ms. McCabe had numerous disorders "strongly associated with dysregulation of inflammatory cytokines and chemokines central to the development of ME/CFS." Id. at 3. She cites exhibit 83 (Vincent C. Lombardi et al., Xenotropic Murine Leukemia Virus-related Virus-associated Chronic Fatigue Syndrome Reveals a Distinct Inflammatory Signature, 25 In Vivo 307 (2011)) as evidence of the inflammatory signature of severely ill CFS patients whose CFS was triggered by an unknown viral illness. Exhibit 81 at 3.

Ms. Mikovits also cites exhibit 84 (Jose G. Montoya et al., Cytokine Signature Associated with Disease Severity in Chronic Fatigue Syndrome Patients, 114 Proc. National Academy of Sciences E7150 (2017)) as further evidence of a "cytokine signature" in CFS patients. Exhibit 81 at 3.

In summary, she says, "whether or not the prior influenza vaccines did or did not contribute to Ms. McCabe's medical status at the time she received the September 11, 2010 vaccination, there is no question that she had been previously sensitized to the components of the influenza vaccines and that the timing of her reaction to the September 11 vaccination was completely appropriate." Id. at 4. The bases for many of Ms. Mikovits' declaratory statements remain unclear.

14. Dr. Levine's Final Report (Exhibit 90)

In her final report, Dr. Levine again reviews parts of Ms. McCabe's medical records, observing that she experienced insomnia three months after her October 2, 2006 flu vaccination. Exhibit 90 at 1. Again, Dr. Levine overlooks Ms. McCabe's treatment for insomnia for some time prior. Dr. Levine also notes Ms. McCabe's diagnosis with gastritis two months after her October 2008 flu vaccination. Id. She concludes "[c]learly, she was sensitized to influenza vaccines and the reaction to that final vaccination was an appropriate temporal relationship." Id. Dr. Levine provides no persuasive reason why this is so.

Dr. Levine, again, states that heightened levels of IL-6 are associated with ME/CFS and other inflammatory diseases. Id. Without citing any literature, Dr. Levine asserts that "[t]he elevated Interleukin-6 levels that I mention in my original report are found by researchers studying ME/CFS patients and account for the abnormal blood brain barrier and thus the cognitive symptoms found in patients with this disease." She also, again, notes that since IL-6 is not used in a clinical setting, it is not surprising that Ms. McCabe never had her IL-6 levels measured. Id.

Dr. Levine's final report presents an "alternative theory" that she believes is "plausible." Id. at 2. She puts forth the possibility that Ms. McCabe had CFS prior to her September 11, 2010 vaccination. Id. In fact, Dr. Levine says it is "likely" that Ms. McCabe had CFS all along. Id. Dr. Levine then asserts that the September 11, 2010 flu vaccine "worsened" her CFS, causing her to be unable to function. Id.

Dr. Levine concludes by saying that "[t]he symptoms Ms. McCabe experienced within six hours and in the subsequent days following the September 10, 2010 Flu Vaccination, completely support the appropriate temporal sequence of ME/CFS significant aggravation". Id. Again, no support is given for this statement beyond her ipse dixit about it being an "appropriate temporal sequence."

15. Concerns Raised on September 6, 2017

Ms. McCabe submitted her pre-trial brief on September 5, 2017. Her witness list did not include Dr. Axelrod.

In an order dated the next day, the undersigned identified numerous issues with the brief and directed Ms. McCabe to file a revised version of the document. Order, issued Sep. 6, 2017, at 1. Chief among the undersigned's concerns were: 1) It was not clear if Ms. McCabe believes she had CFS before the vaccination; 2) Insufficient factual development of Ms. McCabe's current condition; 3) A lack of evidence about how one would expect CFS to develop in the absence of the vaccination; 4) An insufficiently developed medical theory linking the vaccine to CFS; and 5) The lack of evidence pertaining to the appropriate timing between the vaccine and the onset, or worsening of, her CFS. Id. at 2-3. The undersigned also stated a concern that the lack of testimony from Dr. Axelrod would undermine the weight of Ms. Mikovits' and Dr. Levine's testimony because they both adopted his opinions in their reports. Id. at 3.

Ms. McCabe filed a revised pre-hearing brief on September 11, 2017. The Secretary filed his brief on September 29, 2017. At the same time, the Secretary filed the final reports from Dr. Whitton and Dr. Matloubian. Exhibit K; exhibit L.

16. Dr. Whitton's Final Report (Exhibit K)

Dr. Whitton began his report by questioning Ms. Mikovits' previous statement that she had "submitted voluminous literature including a 2014 book chapter . . . that included 153 references to the potential role of inflammatory cytokines generated by vaccines in acting as a necessary trigger for the initiation and progression of disease." Exhibit K at 1 (citing exhibit 81 at 1). Dr. Whitton states that he has reviewed the material and "neither that chapter, nor any of the 153 references therein, provides any reliable scientific data regarding the cytokine responses of humans in response to influenza vaccination." Exhibit K at 1. Dr. Whitton specifically points out that the chapter contains only two references to vaccinations at all and that neither reference to vaccination is supported by a reference. Id.

Dr. Whitton comments favorably on petitioner's exhibit 84 (Montoya) and states that the paper does "extend several published studies suggesting that CFS may be accompanied by low-level inflammatory responses." Exhibit K at 1. However, he notes that this paper has nothing to do with vaccines and reemphasizes his previous point that the article, like Ms. Mikovits' previous

reports, fails to "provide any reliable data whatsoever regarding the cytokine responses that occur following flu vaccination." Id. at 1-2.

Dr. Whitton then comments on Dr. Levine's final report. His comment is succinct enough to cite almost in whole:

> Dr. Levine claims that flu vaccine triggered cytokine production that caused disease, but – despite this being her fourth opportunity to do so – she fails to provide any data to support her assertion. The Court will recall that, in previous reports, she based her assertion on the petitioner's report from Dr. Axelrod – a report that I debunked in Exh. C. Moreover, Dr. Levine failed to address a paper that I had cited in Exh. G (my response to her first three reports), in which the authors had explicitly stated that CFS was NOT associated with adjuvanted flu vaccination.

Exhibit K at 2.

17. Dr. Matloubian's Final Report (Exhibit L)

Dr. Matloubian's final report comments on Dr. Levine's previous report (exhibit 90). He stated: "Dr. Levine has not provided any additional information or literature in support of the diagnosis of ME/CFS in the petitioner" and has "failed again to provide a medical theory that is supported by evidence in the literature to link an inactivated non-adjuvanted influenza vaccine to development or exacerbation of ME/CFS." Exhibit L at 1.

Dr. Matloubian again rebuts Dr. Levine's point that Ms. McCabe's "gastritis" is evidence of her ME/CFS. Id. Dr. Matloubian points out that Ms. McCabe was diagnosed with gastropathy, not gastritis. Id. Citing exhibit L2 (M. Feldman & P. Jensen, Classification and Diagnosis of Gastritis and Gastropathy, UpToDate (Dec. 17, 2015), www.uptodate.com)), Dr. Matloubian distinguishes gastritis from gastropathy: "gastritis is predominantly an inflammatory process, while the term gastropathy denotes a gastric mucosal disorder with minimal to no inflammation." Id. Dr. Matloubian adds that gastropathy is associated with the chronic congestion, which Ms. McCabe experienced. Exhibit L at 2.

Dr. Matloubian disagrees with Dr. Levine's statement that Ms. McCabe's insomnia three months following her September 11, 2010 vaccination could be associated with the vaccine. Id. He states that she does not provide any mechanism for elevated cytokine levels being present three months following the vaccination and provides no explanation for how Ms. McCabe's vaccine reaction

could be three months afterwards for the 2006 vaccination and 6 hours afterwards for the 2010 vaccination . Id. This criticism dovetails with a later point Dr. Matloubian raises: "in the absence of even a basic understanding of the cause or consequence of [ME/CFS], it is virtually impossible to attribute causation or exacerbation to a specific event, such as vaccination with any degree of medical certainty." Id. at 3. Similarly, he states, "it is impossible to define the appropriate medical time-frame that an event such as vaccination could allegedly lead to development or aggravation of [CFS]." He concludes: "This likely explains why, despite multiple opportunities to do so, Dr. Levine has been unwilling, or unable, to state what the accepted general timeframe is for vaccine-induced ME/CFS." Id.

18. Concerns Raised on October 4, 2017

A pre-hearing status conference was held on October 4, 2017. The undersigned again raised the concern that, based on the submitted record, a reasonable basis for proceeding to the hearing did not exist. Order, issued Oct. 10, 2017, at 3. The undersigned stated that this concern involved both the question of Ms. McCabe's diagnosis and the issue of causation. Id.

Ms. McCabe requested a ruling, prior to the hearing, on whether reasonable basis existed. Without such a ruling, Ms. McCabe stated a concern that proceeding to the hearing would present a risk of undue hardship. Pet'r's Mot., filed Oct. 6, 2017. As an alternative, Ms. McCabe requested that the hearing, or at least the portion concerning causation, be postponed. Id.

Ms. McCabe's motion was denied. Order, issued Oct. 11, 2017. The undersigned did advise that Ms. McCabe could always voluntarily conclude her case prior to the hearing or move for a decision on the record. Id. Ms. McCabe was ordered to file a status report on her decision regarding how to proceed in this matter. Id. at 3.

On October 13, 2017, Ms. McCabe stated that she intended to proceed with the hearing. A three-day hearing was held on October 18-20, 2017. The period for submitting evidence was closed on October 25, 2017, leaving the matter ripe for adjudication.

III. Standards for Adjudication

Compensation under the Vaccine Act is available in two major forms. Table injuries, which presume causation, can be established if a prescribed injury occurs during a set period of time following a specific vaccination. 42 U.S.C. § 300aa-11(c)(1)(C)(i). Alternatively, petitioners can receive compensation for injuries not

provided for in the Vaccine Injury Table by bringing a successful petition for compensation under 42 U.S.C. § 300aa-11(c)(1)(C)(ii) of the Vaccine Act.

Here, Ms. McCabe does not claim that CFS constitutes a Table injury under the Vaccine Act. As an "off-Table Injury," Ms. McCabe must demonstrate that the vaccine caused her injury.

Petitioner's burden of proof as an off-Table injury is explicitly defined by Congress. The Act provides that a petitioner must show, by a preponderance of the evidence, that the vaccine sustained or significantly aggravated her illness or injury. See 42 U.S.C. § 300aa–13(a)(1) and 42 U.S.C. § 300aa-11(c). See also Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010) (noting that petitioners must prove causation by the traditional tort standard of preponderance). As for what is specifically required to meet this burden, the statute requires that the conclusion of the court or special master may not be "based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion." 42 U.S.C. § 300aa-13. The statute does not speak to the strength or reputability of the medical opinion, just that a medical opinion or medical records are necessary for a claim to be meritorious. Id.

In drawing conclusions on causation, the Federal Circuit has noted that special masters must be careful not to raise petitioners' burden by establishing tests that create requirements not in the statute itself. Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006) (rejecting a test that required "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities"); Althen, 418 F.3d at 1279 (rejecting a test requiring "confirmation of medical plausibility from the medical community and literature" in order to prove causation-in-fact); Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 549 (Fed. Cir. 1994) ("to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program").

Instead, special masters must consider all the evidence and decide whether the causal link between the vaccine and the injury was logical and legally probable. See Knudsen, 35 F.3d at 549 ("The sole issues for the special master are, based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the [] injury."); Grant v. Sec'y of Health & Human Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("Causation in fact requires proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury."); Hines v. Sec'y of

Health & Human Servs., 940 F.2d 1518, 1525 (Fed. Cir. 1991) ("causation in fact requires proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury.").

IV. Analysis

Three major findings, independently, preclude compensation for Ms. McCabe. First, the evidence submitted does not provide preponderant proof that Ms. McCabe suffers from her claimed injury, CFS. Second, the evidence submitted does not present preponderant proof that her overall condition changed following the September 11, 2010 flu shot. This finding also means that Ms. McCabe cannot prevail on a cause of action that the flu vaccine significantly aggravated her CFS. Third, the evidence submitted does not present preponderant proof that the flu vaccine caused Ms. McCabe's injury.

A. Petitioner's Claimed Injury—CFS

Though not explicitly incorporated into the Althen analysis, the Federal Circuit has recognized that implicit in the causation-in-fact analysis is the identification of petitioner's injury. As the Federal Circuit notes, "a careful reading of Althen, shows that each prong of the Althen test is decided relative to the injury." Broekelschen, 618 F.3d at 1346. The Federal Circuit concludes from this that "identifying the injury is a prerequisite to the analysis." Id. This logic was extended in Lombardi to hold that "the statute places the burden on the petitioner to make a showing of at least one defined and recognized injury." Lombardi v. Sec'y of Health & Human Servs., 656 F.3d 1343, 1353 (Fed. Cir. 2011). Any question about the reach of the preliminary analysis envisioned by the panels in Broekelschen and Lombardi was, at least partially, quelled in Hibbard, when the Federal Circuit noted "[i]f a special master can determine that a petitioner did not suffer the injury that she claims was caused by the vaccine, there is no reason why the special master should be required to undertake and answer the separate (and frequently more difficult) question whether there is a medical theory, supported by 'reputable medical or scientific explanation,' by which a vaccine can cause the kind of injury that the petitioner claims to have suffered." Hibbard v. Sec'y of Health and Human Servs., 698 F.3d 1355, 1365 (Fed. Cir. 2012).

Ms. McCabe has not demonstrated that she suffers from her claimed injury—CFS. Given that Ms. McCabe's case hinges on her assertion that she suffers from CFS, her lawyer and her experts should have spent more effort to establish this central fact. This lack of development occurred despite the

undersigned's reminders that Ms. McCabe had not sufficiently established the facts necessary to prove that she suffers from CFS.

Granted, demonstrating that a person has CFS is, in one respect, a difficult task. The underlying pathology of CFS is not known. See generally exhibit M1 (IOM). As a result, there is no "gold standard" test for what is and is not CFS. This has led to the development of multiple criteria, with the IOM noting that no fewer than 20 different ways of diagnosing someone with CFS exist. Id. at 38. This multiplicity could create a challenge if Ms. McCabe were to argue that she met one criteria, while the Secretary were to argue that she failed under another. The task here does not present that challenge since Ms. McCabe—despite there being 20 different criteria to choose from—has not presented a single criteria that indicates that she suffers from CFS.

In another respect, however, establishing CFS is straightforward. Ms. McCabe merely could have presented any recognized set of diagnostic criteria and then attempted to establish facts that show that she meets the criteria. In an order issued on April 10, 2017, Ms. McCabe was directed to have her expert do just that. In response, Ms. McCabe submitted a report from Dr. Levine that said, in relevant part:

> Reference 1 describes:
>
> Page 5 (exclusion of other causes of fatigue, including 'cardiac and pulmonary dysfunction') as was done by normal [chest x-ray] and troponin level (to exclude myocardial infarction)
>
> Page 6 (under last paragraph Canadian ME/CF Case definition); 'short term memory' and 'lightheadedness')
>
> Reference 2 describes:
>
> Under 'B Neurological Impairments' page 329
>
> Short term memory loss'
>
> 'Pain': significant pain'
>
> Sleep disturbances: 'disturbed sleep patterns'

> Under 'C Immune, Gastrointestinal and genitourinary impairments'
>
> 'Nausea' page 330
>
> Thus, the complaints reported by the patient in the above Exhibits match the symptoms and exclusionary criteria contained in the case definitions provided in References 1 and 2.

Exhibit 72 at 2.

It would appear, based on Dr. Levine's analysis, that she diagnosed Ms. McCabe simply by cherry-picking certain parts of the diagnostic criteria (e.g., 'short term memory loss') and matching those terms with some of Ms. McCabe's complaints. This approach to her diagnosis fails for two reasons. First, she failed to present the entire criteria for any definition that she used and, as such, failed to address all of the required elements of the proposed diagnostic criteria. Second, in attempting to satisfy specific elements of the diagnostic criteria, Dr. Levine sometimes failed to address findings from Ms. McCabe's own treating physicians demonstrating that she did not have the impairments that Dr. Levine assumed she did. These points are addressed below.

1. Diagnostic Criteria for CFS

Dr. Levine cites different criteria, never landing on a preferred set. In her report, as quoted above, Dr. Levine refers to two different criteria: "Reference 1" and "Reference 2". Exhibit 72 at 6. "Reference 1" is an article that, briefly, covers the Canadian Consensus Criteria (CCC). "Reference 2" is the International Consensus Criteria (ICC). Although Dr. Levine referenced the International Consensus Criteria, her hearing testimony indicates that she based her conclusion that Ms. McCabe suffered from CFS on the Canadian Consensus Criteria. See Tr. 443-44 (Dr. Levine testifying that this was because she views the CCC as being "more tested in time"). Then, in her testimony, Dr. Levine added a third set — the criteria from the IOM.[17] Because it is not clear which criteria the petitioner

[17] Dr. Levine's delayed discussion of the IOM report was surprising. The IOM issued its report in 2015, making it much more current than either the CCC from 2003 or the ICC from 2011. The IOM is also recognized for the credentials of its members and the quality of its reports. Therefore, it would seem that the 2015 IOM report would be the first stop, not the third.

Moreover, because Dr. Levine's practice is devoted to treating patients with CFS, it would be easy to infer that, as an expert in the field, Dr. Levine would know about the 2015 IOM

embraced, all three criteria are evaluated below. All three diagnostic criteria are divided into inclusionary criteria and exclusionary criteria. The analysis for the exclusionary criteria are relatively homogenous and thus are described together after reviewing the inclusionary criteria for all three first.

a. Canadian Consensus Criteria

The CCC was published in 2003 to provide a working case definition to those making diagnoses of CFS. Exhibit M1 (IOM) at 48. Even though Dr. Levine concluded that Ms. McCabe satisfies the CCC, she never actually presented the criteria. However, the CCC is summarized in the IOM report:

Required Symptoms:

- Fatigue
- Post-exertional malaise (PEM) and/or fatigue
- Sleep dysfunction
- Pain
- Two or more neurological/cognitive manifestations
- At least one symptom from two of the following categories:
    - Autonomic
    - Neuroendocrine
    - immune
- Illness lasting $\geq$ 6 months

Exhibit M1 (IOM) at 42 (Table 3-1).

report. However, even this slight inference is not necessary because Dr. Levine was a reviewer of the 2015 IOM report. Exhibit M1 (IOM) at 9.

Several of these criteria are problematic given the facts. It is not clear that Ms. McCabe can satisfy the requirements of fatigue,[18] PEM, and pain.[19] It is also unclear whether Ms. McCabe has one symptom from two of either autonomic, neuroendocrine, or immune dysfunction.

Resolving whether Ms. McCabe has established, on a preponderance of the evidence basis, these criteria is not necessary however, because she almost certainly does not fulfill another criteria: "Two or more neurological/cognitive manifestations." Two neurologists examined her and found her normal. Exhibit 6 at 4 (Dr. Herbstein); exhibit 8 at 5 (Dr. Forster). In addition, a neuropsychologist also found her normal. Exhibit 8 at 19 (Ms. Borod, Ph.D.). The evaluations from these professionals weigh more heavily than Ms. McCabe's testimony that she suffers from short term memory loss and other cognitive symptoms. See Capizzano, 440 F.3d at 1326 (noting the importance of contemporaneously created medical records). As a result, Ms. McCabe cannot satisfy the CCC on this basis alone.

b. International Consensus Criteria

Dr. Levine also references the International Consensus Criteria (ICC). See exhibit 62 (Carruthers). The ICC was published in 2011 and was developed using the CCC as a foundation, but made "significant changes." Id. at 328. While the ICC now calls the condition Myalgic Encephalitis (ME) as opposed to CFS, it appears that 1) this decision was not without criticism, and 2) that it is ultimately a

[18] While it is undisputed that Ms. McCabe had long-standing fatigue, different CFS criteria require different levels of fatigue. For example, the revised CCC requires a "substantial reduction in functioning." Exhibit M1 (IOM) at 72. Dr. Levine said that in evaluating her patients to see if the level of fatigue reaches the level necessary for a diagnosis of CFS, she has them complete a questionnaire, filed as exhibit 91. Exhibit 90 at 2.

As explained in more detail below, see Section IV.B, Ms. McCabe did not present persuasive evidence that her functioning was substantially reduced. For instance, Ms. McCabe never completed Dr. Levine's questionnaire. The same general critique is true for whether Ms. McCabe experiences PEM.

[19] Ms. McCabe periodically reported pain. But, as respondent points out, Ms. McCabe's pain has been associated with degeneration in her back. Exhibit H at 2 ("The petitioner had other explanations for her musculoskeletal complaints, such as back pain, which could be related to the documented degenerative joint disease affecting her spine."). See also exhibit A at 9 ("Ms. McCabe has known multilevel degenerative disk disease in cervical, thoracic, and lumbar spine and osteoporosis which were known to be present before September 11, 2010 and which are expected to cause intermittent or more enduring symptoms."). As noted in Section IV.A.1.d, a known etiology for certain symptoms can preclude their use as being indicia of CFS.

matter of semantics. For ease of consistency, this decision will continue to refer to the condition as CFS.

The ICC, as an initial matter, requires that a patient have symptoms that result in a substantial reduction in activity compared to premorbid activity levels. A 50 percent reduction is only considered "mild." Id. at 329. Based on the record, it is not clear if Ms. McCabe experienced such a decrease in her activity levels. See footnote 18, above. Beyond this, the ICC also requires:

- Post-exertional neuroimmune exhaustion (PENE)
- At least one symptom from three of the following four neurological impairment categories:
    - neurocognitive impairments
    - pain
    - sleep disturbance
    - neurosensory, perceptual, and motor disturbances
- Immune, gastrointestinal, and genitourinary impairments. At least one symptom from three of the following five categories:
    - flu-like symptoms
    - susceptibility to viral infections with prolonged recovery periods
    - gastrointestinal tract
    - genitourinary
    - sensitivities to food, medications, odors, or chemicals
- At least one symptom from energy production/transportation impairments:
    - cardiovascular
    - respiratory
    - loss of thermostatic stability
    - intolerance of extremes of temperature

Id. at 329-31.

Dr. Levine asserted that Ms. McCabe met this definition because Ms. McCabe had short term memory loss, pain, sleep disturbances, and nausea. Exhibit 72 at 2. Dr. Levine does not explicitly explain how these four items fulfill the criteria. Even without this explanation, it seems readily apparent that Ms. McCabe does not fulfill all the criteria. For example, the neurologists' and neuropsychologist's records indicate that Ms. McCabe does not have a neurocognitive impairment. Dr. Levine also did not cite any medical record indicating that Ms. McCabe suffered from "neurosensory, perceptual, and motor

disturbances." Therefore, it appears that Ms. McCabe did not fulfill the second criteria of the ICC.

c. Institute of Medicine Criteria

The third criteria Dr. Levine referenced is the IOM criteria for CFS. Dr. Levine actually served as a reviewer for the IOM report, which she testifies, constitutes "the latest case definition of this illness." Tr. 276.

The IOM criteria benefits from a certain simple elegance compared to the other criteria. A diagnosis of CFS is satisfied when a patient demonstrates (i) a substantial decrease in function, (ii) that decrease persists for greater than 6 months, (iii) is characterized by post-exertional malaise and unrefreshing sleep, and (iv) the patient has either 1) a cognitive impairment, or 2) orthostatic intolerance. Exhibit M1 (IOM) at 210.

As stated above, the records do not demonstrate that Ms. McCabe has a cognitive impairment. Every neurological exam in the record returns a normal result. Thus, for Ms. McCabe to fulfill the IOM criteria, she must establish "orthostatic intolerance."[20, 21]

Ms. McCabe did not persuasively establish that she has "orthostatic intolerance." Preliminarily, Ms. McCabe did not identify any reports from treating doctors diagnosing her with orthostatic intolerance. As a result, she had Dr. Levine interpret the notes in the record and, based on those notes, provide an opinion that Ms. McCabe had orthostatic intolerance. See Pet'r's Revised Br. at 22 ("Ms. McCabe [was diagnosed with] Sinus Tachycardia which is Postural Orthostatic Tachycardia (POTS)"). Dr. Levine expanded on this conclusion in her testimony. When asked if Ms. McCabe "probably has POTS," she responded:

A. Yes, POTS, right, is an -- and let me just explain that briefly. POTS has to do with reduced cardiac output, and so what happens is

[20] This assumes that Ms. McCabe demonstrated the other criteria, including "a substantial decrease in functioning" and "post-exertional malaise."

[21] Orthostatic intolerance is a general term that can refer to a wide range of manifestations thought to be attributable to autonomic dysfunction. One of these is postural orthostatic tachycardia syndrome (POTS), which is specifically associated with patients trying to sit or stand upright and experiencing an increase in heart rate as a result. Tr. 279. Although the IOM criteria is more general to all types of orthostatic intolerances, petitioner specifically focuses on POTS and, accordingly, that is the focus here. Tr. 290-91.

there's a racing heart, there's increased pulse rate, which was in her record. Ms. McCabe, according to one of the entries, exhibited sinus tachycardia, and also had, you know, swollen legs, and that's related to what we call venous pooling, meaning that because the heart is trying very -- working very hard to try to circulate blood throughout the body, it fails to -- you know, the failing pressures are diminished in the right side of the heart and there's venous pooling. There's sort of an inadequate circulatory response, basically.

Q. And what would you have to do to confirm a diagnosis of POTS?

A. And also the fact that she wears compression stockings, you know, and that's one of the treatments we have for that. To confirm the diagnosis, we send people first -- it's two ways: We now having something called a lean-to test, which is something that clinicians perform in their office and we'll try sometimes, too. And that just involves having the patient lie supine on the exam table, record their blood pressure and pulse, have them sit up very slowly, record blood pressure and pulse, and then have them stand without shifting their feet for 10 minutes and record blood pressure and pulse. And there's a wide -- the pulse usually becomes very elevated, that's why they call it postural orthostatic tachycardia, and then the blood pressure may or may not drop.

Tr. 290-92. Based on Dr. Levine's testimony, it appears that her only basis for concluding that Ms. McCabe has POTS is Ms. McCabe's medical record of sinus tachycardia and that she wears compression stockings, which are also used to treat patients with POTS. When asked, Dr. Matloubian had the following to say about Dr. Levine's testimony and Ms. McCabe's statement that sinus tachycardia is equivalent to POTS/orthostatic intolerance:

A. Having tachycardia I don't think satisfies for orthostatic intolerance.

Q. Why not?

A. Because you can -- anything -- pain can [cause] tachycardia. Anxiety can cause tachycardia. I probably have it right now because I'm on the stand. But, you know, having tachycardia by itself is -- so I have not heard the description -- so what orthostatic intolerance is is

that somebody gets up from a sitting position or a lying position, and that's when the blood pressure drops and the heart rate goes up to maintain that blood pressure. It's a description that people – people describe to their doctors or to other people, and I haven't seen that in the medical records and I haven't heard of it. And then, I think, to continue on that theme, I think Dr. Levine actually attributed leg swelling to a cardiac problem and a sign of orthostatic problems. So I went through the records -- so, since we are on that issue, I think I should talk about it now. So I went through the records, and she was seen by two cardiologists, Exhibit 100 at 81 and -- and I forgot the name of the cardiologist --

Q. Would that be Zaza Alvazi?

A. I think so, yes. So -- so Exhibit 100 at 81, and on physical exam, she notes there's no edema, and that was, I think, in 2016.

Q. So, for the record, looking at that exhibit – do you have that in front of you?

A. Ah, I can pick it up. So this is dated 2/15/2017, new patient, I think it was for chest pain, no swelling of the feet, no swelling of the ankles, no swelling -- no mention of edema on the exam. And then there was an echo done, echocardiogram, a transthoracic echo on 2/15/2017, which is Exhibit 105 at 5, and there was no abnormality of cardiac function.

Tr. 675-76.

In conclusion, the records show that Ms. McCabe was never diagnosed with POTS or complained of symptoms specific to a diagnosis of POTS. The lack of a diagnosis is especially salient given how simple the test for POTS is, as Dr. Levine testified. Furthermore, the evidence that is in the record shows that Ms. McCabe has normal cardiac function, which is, at the least, inconsistent with a finding of POTS, though not dispositive. This finding, in combination with the weight of the evidence showing no cognitive impairment, appears to preclude a finding of CFS under the IOM guidelines.

d. Exclusionary Criteria for Diagnosis of CFS

So far, the focus of the analysis has been under the inclusionary criteria used by the CCC, the ICC, and the IOM in diagnosing CFS. However, all three criteria embrace the use of exclusionary criteria, although to different extents. In the case of the CCC, a diagnosis of certain diseases, such as sleep apnea, per se precludes a diagnosis of CFS. Exhibit M1 (IOM) at 44. In the case of the ICC and IOM, sleep apnea is not an automatic exclusion. Instead, the authors of the ICC explain:

> As in all diagnoses, exclusion of alternate explanatory diagnoses is achieved by the patient's history, physical examination, and laboratory/biomarker testing as indicated. It is possible to have more than one disease but it is important that each one is identified and treated. Primary psychiatric disorders, somatoform disorder, and substance abuse are excluded.

Exhibit 62 at 5. The IOM appears to adopt a similar approach, stating that it is necessary to identify comorbid conditions so that it can be determined whether they are accounting for the symptoms that may be associated with CFS. See exhibit M1 (IOM) at 247. In other words, a diagnosis of CFS is not appropriate under any of the guidelines if Ms. McCabe has another condition that, when treated, accounts for her symptoms.

Ms. McCabe was, at least, twice referred for a sleep study. Tr. 127. Ordering a sleep study for patients complaining of fatigue appears to be standard practice. Dr. Levine testified that "if [her patients] have complaints of persistent fatigue, I will send a patient for a sleep study to determine whether they have sleep apnea." Tr. 326. This is consistent with Dr. Matloubian's practice, as he testified:

> I ask them if they get unrefreshing sleep and whether or not, you know, when they get up in the morning they feel like they're hit by truck or they're okay, and I recommend or send them myself for a sleep study to rule on the obstructive sleep apnea. So without that being addressed, I – you know, I -- I can't say that she meets that – that that's because of this chronic fatigue syndrome.

Tr. 674.

Ms. McCabe, however, never went for her sleep study. Tr. 127. As Dr. Matloubian explained, this is especially important for Ms. McCabe because she has

or has complained of snoring, sinusitis, GERD, bronchiectasis, and COPD, all of which can be aggravated by sleep apnea. Tr. 674. Given that performing a sleep study appears to be the first diagnostic step when patients complain of fatigue, it is puzzling that Ms. McCabe has not had one performed. Regardless of the explanation for why that is, it appears premature to find that Ms. McCabe suffers from CFS, under any criteria, without it.

Ultimately, Federal Circuit precedent tasks special masters with determining whether petitioners present preponderant evidence that they suffer from the disease for which they are claiming compensation. See Lombardi, 656 F.3d at 1355; Broekelschen, 618 F.3d at 1346. The very fact that no treating doctor of Ms. McCabe's diagnosed her with CFS weighs against a finding that Ms. McCabe has CFS. However, Ms. McCabe could overcome this by presenting expert testimony that makes a persuasive showing that the petitioner does, in fact, suffer from the claimed injury. However, Dr. Levine's testimony was not persuasive. Thus, and for the reasons elucidated above, the evidence does not favor a determination that Ms. McCabe has met her burden.

B. Significant Aggravation

In her amended petition, Ms. McCabe claimed, in the alternative, a cause of action that the flu vaccine significantly aggravating her CFS. It is, perhaps, true that the previous analysis precludes compensation for her significant aggravation claim since her failure to establish that she has CFS makes it, it would seem, impossible to show that her CFS was significantly aggravated. Lombardi, 656 F.3d at 1353 ("In the absence of a showing of the very existence of any specific injury of which the petitioner complains, the question of causation is not reached").

However, because diagnoses such as CFS are somewhat amorphous, it appears prudent to examine if, regardless of the specific diagnosis, her overall condition changed following the September 11, 2010 vaccination. Comparing a vaccinee's condition before and after vaccination is essentially equivalent to the beginning portion of the test for significant aggravation established by the Federal Circuit. Specifically, the Federal Circuit has held that to establish significant aggravation, petitioners must show: "(1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a 'significant aggravation' of the person's condition prior to vaccination" W.C., 704 F.3d at 1357. The Vaccine Act defines significant aggravation as "any change for the worse in a preexisting condition which results

in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." 42 U.S.C. § 300aa-33.

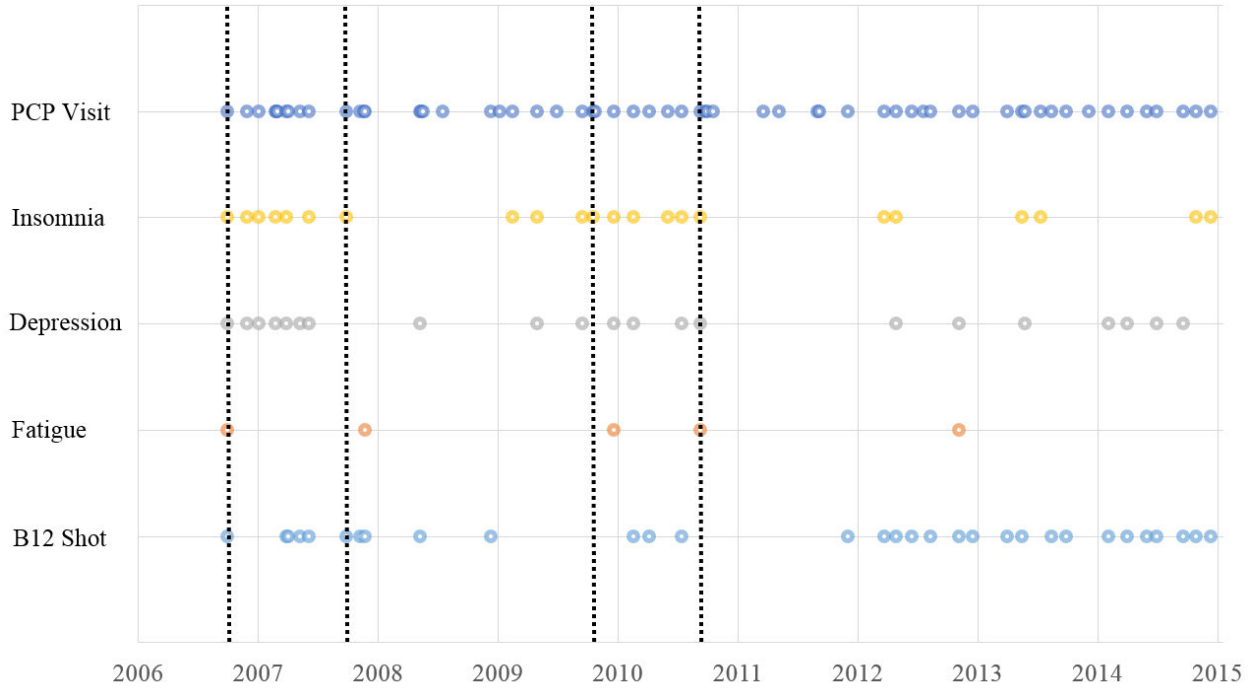
Ms. McCabe testified that the vaccination on September 10, 2010 marked a dramatic change in her life. Proving this difference is Ms. McCabe's burden. She attempted to meet this burden by proffering medical and employment records, and her own testimony. Both the records and the testimony fail to make a persuasive case that she experienced any marked change in her condition following the September 10, 2010 flu vaccine.

1. Records

In determining Ms. McCabe's health before and after the vaccination, the starting point is the collection of medical records. "Medical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." Cucuras, 993 F.2d at 1528.

The medical records do not support Ms. McCabe's claim that the vaccination marked a turning point in her health. The records submitted in this matter date back to October 2, 2006 and run through the month of the hearing. Section I set forth the details of the medical records. As discussed there, the records show a consistent reporting of the same symptoms: depression, insomnia, and fatigue. Often fatigue is not noted explicitly, although Ms. McCabe testified she requested B12 shots to address her fatigue. Tr. 64. B12 shots were requested and administered on almost every visit.

Looking for changes in the reporting of her symptoms by reading through the visits themselves is somewhat difficult. The figure below graphically presents all incidents of Ms. McCabe reporting depression, insomnia, fatigue, or receiving a B12 shot during her visits to her primary care physician (PCP). The dates range from the first submitted record from October 2, 2006 (four years before the 2010 vaccination) to the end of 2014 (four years after the 2010 vaccination). The documented flu shots are indicated by vertical dashed lines, with the right-most one representing the September 11, 2010 shot. The medical records, on their own, cannot sustain the conclusion that the 2010 flu vaccination marked the onset, or significant aggravation, of her condition.



Ms. McCabe also had the opportunity to prove her case through other contemporaneously created supporting documents, such as employment records. The employment records are potentially useful because if a person were ill (or fatigued), the person may miss time from work.

Ms. McCabe was directed to file her employment records. Order, issued Apr. 29, 2014. Ms. McCabe filed employment records only from Wankel Hardware, where Ms. McCabe worked part-time to complement her nursing work. Exhibit 14; Tr. 94. The Wankel Hardware records date back to the July-September quarter of 2009. They show the following payment amounts per quarter:

Pay Period	**Gross Wages ($)**
July – Sep. 2009	2500
Oct. – Dec. 2009	2450
Jan. – Mar. 2010	2400
Apr. – June 2010	650
July – Sep. 2010	983
Oct. – Dec. 2010	**3547**
Jan. – Mar. 2011	2601
Apr. – June 2011	3311
July – Sep. 2011	2838
Oct. – Dec. 2011	3547
Jan. – Mar. 2012	2601
Apr. – June 2012	3311
July – Sep. 2012	2838
Oct. – Dec. 2012	3784
Jan. – Mar. 2013	2838
Apr. – June 2013	3311
July – Sep. 2013	2838
Oct. – Dec. 2013	3784
Jan. – Mar. 2014	2838

Exhibit 14. The bolded line is the pay period following her vaccination. In the Oct. – Dec. 2010 quarter, Ms. McCabe earned more money than any other period through that date. The Oct. – Dec. 2010 quarter remains one of her highest pay periods from her entire time at Wankel. The evidence from this employer thus not only cannot sustain a claim that she suffered a change in health following the September 11, 2010 flu vaccine, but appears to contradict it directly.

Her income from Wankel Hardware was not her only source of income during this period. Ms. McCabe testified, and included in her affidavits, that during the time she was at Wankel, and to this date, she worked part-time as an in-home nurse's aide to private clients. Tr. 94-96; exhibit 13. She further testified that she only worked in temporary positions as an in-home nurses' aide following the September 11, 2010 vaccination. Tr. 96. Unfortunately, Ms. McCabe does not recall her work during this time period with any specificity and even failed to remember, or refused, to name her employers. Tr. 95. This makes evaluating her reduction in work as a nurses' aide nearly impossible.

However, her gross earnings both before the vaccination and today provide some insight into her overall employment levels. She stated that, as of today, her earnings are "usually . . . 30,000." Tr. 96. This income comes completely from work as a nurse's aide because she no longer works at Wankel. Tr. 89-90. In comparison, in her affidavit dated May 2, 2014, she reported "companion care" income prior to the vaccination of approximately $18,000 that complemented her income from Wankel of approximately $13,000. Exhibit 13 at 1. Thus, before the vaccination she worked part time as an in-home aide, making $18,000. Her part-time employment today results in a take-home of $30,000. While we are lacking in specifics, the evidence concerning income is not consistent with a finding that Ms. McCabe's employment was affected by the September 11, 2010 vaccination.

2. Testimony

Although the medical records and employment records corroborate each other in showing that Ms. McCabe's health and activity level were relatively similar before and after vaccination, Ms. McCabe introduced another form of evidence — her testimony. However, against her medical and employment records, Ms. McCabe faced an uphill climb in demonstrating that the administration of the flu vaccine corresponded with a significant change in her condition. As the Supreme Court has noted: "[w]here [oral testimony] is in conflict with contemporaneous documents we can give it little weight." United States v. U.S. Gypsum Co., 333 U.S. 364, 396 (1948).

In guiding the evaluation of the persuasiveness of Ms. McCabe's testimony, the undersigned made impressionistic determinations about the credibility of her statements. See Tweten v. Sec'y of Health & Human Servs., 26 Cl. Ct. 405, 410 (1991) ("Credibility findings are by nature impressionistic"). Though it may be more tactful to publish this decision without overtly stating these assessments, doing so appears unadvised by the appellate courts of this Program, which explicitly rely on special masters' ability to evaluate live witnesses' statements. See Bradley v. Sec'y of Dep't of Health & Human Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993) ("The fact-finder has broad discretion in determining credibility because he saw the witnesses and heard the testimony.")

Ms. McCabe's testimony was neither credible nor persuasive. Earlier in this decision, the undersigned reviewed Ms. McCabe's recollections about her quality of life prior to the September 11, 2010 vaccination. See Section I.B, above. Ms.

McCabe consistently painted a positive picture of her life prior to the 2010 vaccination. This included descriptions such as:

> " . . . [I] did not have any recurring health problems." Exhibit 13 at 1.
>
> " . . . [I] was very active." Exhibit 91 at 1.
>
> "Prior to September 11, 2010, I was very active. . . . I had no problems with stamina. . . . I was always on the go." Exhibit 91 at 1.
>
> "Everything was great. . . . everything was just 100 percent." Tr. 17.
>
> "I was always on the go. It would take a lot to hold me down." Tr. 41.

Her testimony is the only evidence offered in support of these claims. However, her testimony about her life before the vaccination cannot be credited in the face of such overwhelming contrary evidence found in Dr. Kang's records and in the limited information we have about her employment. Even Ms. McCabe's own expert, Dr. Levine, concluded that Ms. McCabe's health was not dramatically different before and after the vaccine. Tr. 313 ("if it were my own records, I would have more certainty, but, you know, judging from my putting together those records, yes, I would say to a greater degree of certainty that she did have it all along").

In addition to the stark contrast between the contemporaneously created records and her testimony, multiple inconsistencies in her testimony further reduced the value that could be given to it.

One example of an inconsistency concerned her travel to Ireland. During the beginning of her testimony, Ms. McCabe stated that following the flu vaccination, she could not travel back to Ireland since the 2010 flu vaccine was given. Tr. 43. ("So I couldn't fly. Before, I'd be home as a regular occurrence, always went home to see my mother and my family."). This testimony was consistent with her September 11, 2017 affidavit, which stated: "As I said, I have been unable to travel, therefore not able to see my mother or attend the funeral of my best friend in Ireland. My life has been completely turned upside down." Exhibit 91 at 2. However, a 2015 medical record from her ophthalmologist recorded under history of present illness: "New headache x 3 days. Was feeling OK since December. Went to Ireland and returned." Exhibit 98 at 17. Towards the end of her

testimony, the undersigned asked Ms. McCabe about this record and how many times since the vaccination she had been to Ireland. Ms. McCabe responded:

> Well, I've gone back using a wheelchair at the airport to get on the plane and get off, and I go back a few times -- not a few times, but pretty much every year after that, but I use a wheelchair to get to the airport -- you know, to get to the plane and a wheelchair to get off the plane.

Tr. 120. Thus, in one version of events, she has not returned to Ireland after the 2010 vaccination, but in another version of events, she has returned to Ireland "pretty much every year."

Another inconsistency concerns depression and menopause. As recited earlier, Ms. McCabe's treating doctor, Dr. Kang, frequently noted that she was depressed before receiving the flu vaccine. See exhibit 1 at 1-12. Ms. McCabe attributed her depression prior to the flu vaccination to menopause:

> Q. Do you recall what was causing depression? Were you having depression at that -- that's throughout the records.
>
> A. Well, basically I think it was to do with – the depression was basically to do with menopause, I think, that's why I was on depression pills . . . .

Tr. 20.

However, in the VAERS form completed in the months after the September 11, 2010 vaccine, Ms. McCabe reports having been pre-menopausal at the time. Exhibit 1 at 87. It seems likely that in 2010, when Ms. McCabe was submitting information to VAERS, she would know whether she was experiencing regular menstrual cycles.

In any event, menopause does not appear in her medical records until 2013. Exhibit 100 at 15. Despite that, depression had been noted consistently throughout the seven years of records covering the period between 2006 (the earliest filed medical record) to 2013 (when menopause was first mentioned). See exhibit 1; exhibit 100. Consistent with Ms. McCabe's testimony, fluoxetine (Prozac) appears to have been prescribed beginning with the onset of menopause. Exhibit 100 at 15. However, this was in 2013, not in 2006.

A third set of inconsistencies concerned Ms. McCabe's description of her condition. After Ms. McCabe had retained three experts and the third expert (Dr. Levine) diagnosed Ms. McCabe with chronic fatigue syndrome, Ms. McCabe was directed to file a new affidavit to disclose her anticipated testimony. See order, issued Sept. 6, 2017. In this affidavit—filed a month prior to the hearing—Ms. McCabe first mentioned "extreme fatigability." Exhibit 91 (signed Sept. 11, 2017). Then, throughout the hearing, Ms. McCabe talked about "unrefreshing sleep." See Tr. 21, 41, 66, 134.

Ms. McCabe's focus on establishing that she had unrefreshing sleep is not surprising given that, as Ms. Mikovits testified, "[t]he hallmark of ME/CFS is an unrefreshing sleep." Tr. 228. Ms. Mikovits described unrefreshing sleep as a phenomenon where people are able to sleep but the sleep does not have the same effect it usually has, where individuals wake up feeling "refreshed." Id. ("It doesn't matter how much these people sleep. When they wake up, they're just as tired.").

From the undersigned's observation of Ms. McCabe's demeanor on the stand, the undersigned cannot credit Ms. McCabe's testimony about "unrefreshing sleep." The frequency with which she used this term in her testimony is vastly different than her previous accounts. If she were having "unrefreshing sleep," she would have told a doctor who would have recorded this complaint in some medical record. While many medical records (before and after the vaccination) refer to fatigue, no medical record discusses "unrefreshing sleep." Similarly, if Ms. McCabe's condition following the flu vaccination was newly hallmarked by overwhelming fatigue, she would have emphasized this problem in the affidavits she filed early in the litigation. Instead, it appears that only after a doctor she retained for litigation diagnosed her with CFS, Ms. McCabe started to use the lingo "unrefreshing sleep." Her references to "unrefreshing sleep" in her live testimony often struck the undersigned as rehearsed and forced for the purpose of litigation. Ms. McCabe's references to "unrefreshing sleep" did not ring true.

The undersigned's impression of Ms. McCabe's testimony regarding her sleep was buttressed by inconsistencies in her testimony. When Ms. McCabe was asked if her fatigue caused her problems before the vaccination, she responded "No, no, because I would be sleeping at night, so I was able to go." Similarly, when asked what it's like when she wakes up from sleep now, she stated: "I have insomnia, so I can't -- I could take an Ambien and I could be awake all night." Tr. 41. This later characterization is more consistent with the medical records and her

early affidavits, which never mention unrefreshing sleep, but do show that she suffers from insomnia and takes Ambien to address it.

It is puzzling, especially in light of Ms. McCabe's testimony, that she failed to provide a single percipient witness that could corroborate her allegation that the September 2010 flu vaccine resulted in a dramatic change in her day-to-day life. She testified that she has a group of friends on whom she has relied since the vaccination for monetary support (Tr. 42) and for assistance with her day to day activities, such as travelling to medical appointments (Tr. 106), providing meals (Tr. 84), and doing chores like laundry (Tr. 85). Ms. McCabe also did not provide any testimony from supervisors who could have recounted how she reduced her work schedule due to fatigue. The absence of any other witnesses was noticeable.

In total, there is simply no evidence that provides any persuasive indication that the September 11, 2010 flu vaccine was associated with a change in Ms. McCabe's condition. Therefore—regardless whether she satisfies the diagnosis for CFS—Ms. McCabe's claim for compensation must fail.[22] This finding, by itself, is sufficient to preclude Ms. McCabe's compensation. Nevertheless, the petitioner's claim of causation is examined lest the absence of discussion would incorrectly imply that causation could be found.

C. Causation

If Ms. McCabe had established her health deteriorated after the vaccination, she would also need to establish, on a more likely than not basis, that the vaccination caused the change. To establish causation under the Vaccine Act, the Federal Circuit has set forth a three-part framework. As explained in Althen, and subsequent opinions, petitioners must put forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing

[22] Ms. McCabe has not demonstrated her entitlement compensation under either a "causation-in-fact" or significant aggravation cause of action. Both theories of relief are based upon a change in health either from no disease to disease (causation-in-fact) or from moderate disease to worse disease (significant aggravation). Here, the evidence preponderates in favor of finding that Ms. McCabe's health stayed relatively the same.

of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.[23] These steps are evaluated below.

1. Althen Prong One: Petitioner's Medical Theory

Despite multiple petitions, nine expert reports from petitioner's experts, two pre-trial briefs, and three days of testimony, Ms. McCabe failed to present a clear picture of how Ms. McCabe's September 11, 2010 flu vaccine caused or significantly aggravated her CFS. Because a causal theory is usually the crux of a petitioner's case, this failure on the part of Ms. McCabe and her team is especially glaring.

Ms. McCabe appeared to switch between two different theories linking the flu vaccine and CFS. In one theory Ms. McCabe argues that the flu vaccination(s) resulted in immune dysregulation, which resulted in CFS. In another, Ms. McCabe claims that the flu vaccination(s) resulted in neurological damage as a result of multiple low-intensity stimulations of parts of her brain, resulting in long-term damage that accounts for her CFS symptoms. This second theory is referred to as "kindling." It is not clear to what extent these theories are mutually exclusive, or completely overlapping. They are addressed in turn.

a. Immune Dysregulation Theory

Ms. McCabe's revised pre-hearing brief sets out perhaps the clearest statement of petitioner's medical theory. She states that:

> Drs. Mikovits' and Ruscetti's theory is that the September 11, 2010 influenza vaccination significantly exacerbated or aggravated the active preexisting inflammatory disease. [They] proposed that over activation and dysregulation of cytokines, chemokines and inflammatory mediators caused synergistic antigenic stimuli and immune mediated damage.

Pet'r's Revised Preh'g Br. at 27.

Thus, petitioner's medical theory appears to have two steps. The first step is the link between the vaccination and immune dysregulation. The

[23] The three Althen prongs correspond, with insignificant changes in wording, to the final three prongs for significant aggravation. For simplicity, this decision refers to them as the "Althen" prongs.

second is the link between the immune dysregulation and the CFS. In her testimony, Ms. Mikovits confirmed that this two-step conceptualization was an accurate rendition of her theory. Tr. 256-57.

Ms. McCabe does not need to prove with scientific certainty that the vaccination she received can cause immune dysregulation or that immune dysregulation can cause CFS. However, petitioners may not posit just any theory of causation; the theory must be "reputable." Althen, 418 F.3d at 1278 ("A persuasive medical theory . . . being supported by reputable medical or scientific explanation") (internal citations omitted). What makes a theory "reputable" is not exactly clear. In Hibbard, the Federal Circuit stated that petitioner's burden was to provide a "viable medical theory by which a vaccine can cause the injury claimed by the petitioner." Hibbard, 698 F.3d at 1365. In contrast to mere "viability," in Moberly, the Federal Circuit required that the theory be "legally probable." 592 F.3d at 1322. Though the Federal Circuit has not spoken in unison about what exactly is required from petitioners, based on the directives it has provided, it appears accurate to say that petitioner's medical theory linking the vaccine and the injury must, at the least, be consistent with what is known about human biology. Without a theory that passes that barrier, the Federal Circuit dictates that compensation should be precluded. If the theory meets this minimum barrier to entry, the special master should proceed to consider the other Althen elements in order to make an ultimate conclusion on the question of whether preponderant evidence exists to conclude causation.

Upon examination, the two steps of Ms. McCabe's medical theory nicely illustrate the different gradations of proof that the Federal Circuit appears to be referencing in their opinions refining the meaning of the first Althen prong.

Beginning with the second step, there is reason to believe that cytokine and other immune cell dysregulation is linked to CFS. As the IOM report noted, some studies have found natural killer (NK) cell dysfunction in ME/CFS patients. Exhibit M1 (IOM) at 152. However, causation has never been demonstrated. Id. It very well could be that the ME/CFS is causing the dysregulation of the NK cells. Similarly, many have hypothesized that cytokine dysregulation causes ME/CFS. Some studies have found correlations, others have not. Id. at 150-151. One paper, that experts from both parties favorably regarded, found that there were a number of cytokines for which their levels were associated with either 1) having ME/CFS or 2) the severity of a patient's CFS. Exhibit 84 (Montoya). Again, it is recognized that this is not proof of causation. Based on findings such as these, the IOM has concluded that NK dysregulation can serve, at the least, as a biomarker

for ME/CFS illness severity, but that more research is necessary to examine the link between ME/CFS and cytokine dysregulation in terms of causality. Exhibit M1 (IOM) at 152.

The evidence linking immune dysregulation and CFS parallels the evidence linking the DPT vaccine and neurological injury in Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1380 (Fed. Cir. 2009). Petitioners in Andreu presented evidence from several studies showing, at the least, a correlation between the two. Id. Importantly, however, scientific proof that DPT causes neurological injury did not exist. Id. Nonetheless, the Federal Circuit emphasized that in examining the proffered theory of causation, special masters must weigh the evidence through the "vantage point of the Vaccine Act's preponderant evidence standard" and not require attribution of causation. Id.

Here, as in Andreu, Ms. McCabe has not demonstrated that it is medically accepted that immune dysregulation can cause CFS. However, the evidence is sufficient to conclude that this is a viable theory and that the evidence linking the two is, at the least, reputable. Thus, the second step of petitioner's theory (linking immune dysregulation to CFS) could survive a thorough Althen step 1 analysis.

However, the first step of petitioner's theory does not possess this same characteristic. Petitioner and her experts allege that the flu vaccine caused immune dysregulation—specifically cytokine dysregulation. Pet'r's Revised Preh'g Br. at 27; Tr. 256-57; Tr. 411. There is no evidence in the record that a flu vaccine can cause this type of dysregulation. Ms. Mikovits initially attempts to get around this absence of evidence by arguing that checkpoint inhibitors and monoclonal antibodies are known to cause cytokine dysregulation. Exhibit 40 at 2. That may be true. However, Ms. Mikovits never elucidates why the characteristics of checkpoint inhibitors and monoclonal antibodies speak to the possible effect of the flu vaccine (which is neither). See exhibit C at 9 (criticizing Ms. Mikovits for equating checkpoint inhibitors and the flu vaccine); see also exhibit 58 at (Ms. Mikovits' report in which she did not address Dr. Whitton's criticism other than to say that both vaccines and checkpoint inhibitors stimulate cytokines).

Ms. Mikovits similarly points out that the smallpox vaccination can result in long term effects on the immune system. Exhibit 58 at 4. But, as the smallpox vaccine contains a live virus, the smallpox vaccine seems different from the flu vaccine, which contains an inactivated virus that cannot replicate. See exhibit F at 3 (discussing smallpox vaccine and how it is different from a flu vaccine).

Although the postulate that the flu vaccination can cause dysfunction in the immune system was an essential part of Ms. Mikovits' theory, Ms. McCabe's counsel and her experts did not explain the foundation for the opinion very well. See Pet'r's Br. at 13, Pet'r's Revised Br. at 14-15. Consequently, a relatively large amount of time was spent at the hearing discussing this question with petitioner's experts. Specifically, the undersigned attempted to elicit the basis for the first step of petitioner's theory by asking both Dr. Levine and Ms. Mikovits to identify the basis for their assertion. Tr. 213; Tr. 412. Dr. Levine referenced exhibits 31, 32, 62, 65, 66, and 68. Ms. Mikovits referenced exhibits 32 and 50. Each of these articles is reviewed below. [24]

Exhibit 31 (M. Saurwein-Teissl et al., Whole Virus Influenza Vaccine Activates Dendritic Cells (DC) And Stimulates Cytokine Production By Peripheral Blood Mononuclear Cells (PBMC) While Subunit Vaccines Support T Cell Proliferation, 114 Clinical Experimental Immunology 271 (1998)) is an in vitro study comparing the stimulatory properties of three different types of influenza vaccine on cultured cells. The researchers stimulated cultured cells with the whole virus vaccine for 24 hours and measured a number of cytokine and other immune cell responses. The study found increased secretion of IL-2 and interferon gamma in the cultured cells. The study did not examine IL-6, the cytokine on which the petitioner's experts had focused.

Dr. Levine argues that this article can be extended to show that the vaccination may have caused "a more dysregulated picture and excess of these unwanted pro-inflammatory cytokines." Tr. 427. In response, Dr. Whitton points out that in this study "none of the experiments involve vaccination." Tr. 574. As. Dr. Whitton states "there is no question – let's be absolutely clear – there is no question that vaccines do trigger cytokine production. There's absolutely no doubt about that." The question is immune dysregulation, or in other words "to what level do cytokines ascend, and for how long." Tr. 575. Having evaluated the article, the undersigned agrees with Dr. Whitton that the article does not inform the

[24] Because Dr. Levine and Ms. Mikovits selected these articles, the decision discusses them in great detail. Conversely, this decision does not discuss the articles that Dr. Levine and Ms. Mikovits did not identify. See Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1347 (Fed. Cir. 2010) ("Given that there was no testimony offered by any expert as to the validity or import of such an article for this case, the Special Master did not err in disregarding such evidence, which at best addressed a peripheral issue.") However all the articles have been reviewed, regardless of whether this decision discusses them. See Moriarty v. Sec'y of Health & Human Servs., 844 F.3d 1322, 1332 (Fed. Cir. 2016) (holding that the special master erred by not considering medical records that were not referenced during the hearing).

question of the vaccine's ability to induce immune dysregulation and there is no reason to extend the article to make that conclusion. Based on the content of the article, the authors themselves do not see the article as supportive of that point and Dr. Levine never states a basis for making that conclusion.

Exhibit 32 (Lisa M. Christian et al., Serum Proinflammatory Cytokine Responses to Influenza Virus Vaccine among Women during Pregnancy Versus Non-Pregnancy, 70 Am. J. Reproductive Immunology 1 (2013)) measured the levels of IL-6, and several other compounds, in pregnant and non-pregnant women following an influenza vaccine. Dr. Levine cited exhibit 32 for the proposition that "I think we can at least make the suggestion that those abnormal – those cytokine responses may not return to baseline in patients who have CFS." Tr. 428. Respondent's expert, Dr. Whitton, focused on the article's figure 2. Tr. 576. As displayed in that figure, reproduced below, IL-6 levels were higher than baseline one day following vaccination but returned to normal levels by the second day.

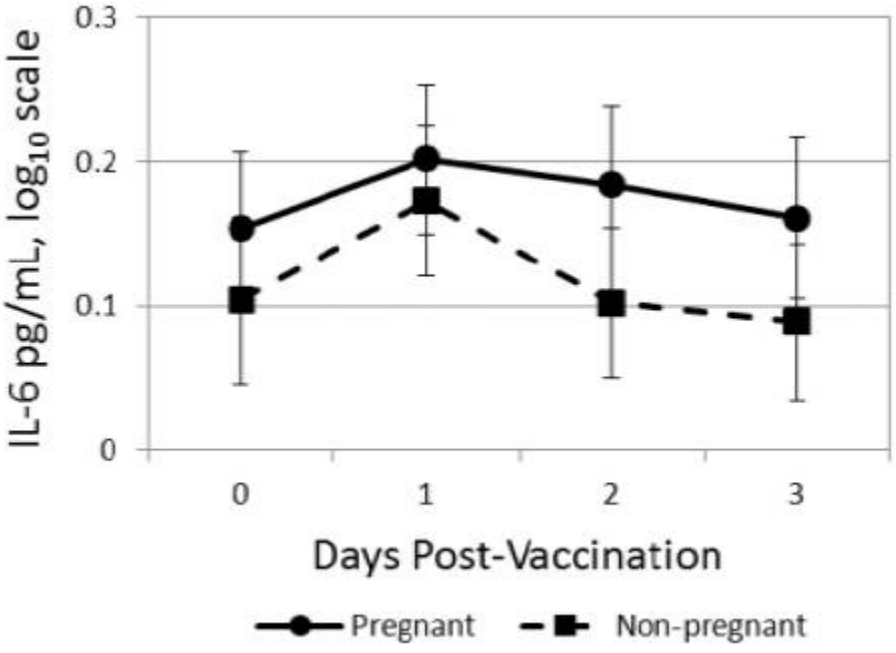


Figure 2 is consistent with Dr. Whitton's assertion that any cytokine-reaction to the flu vaccine is "both limited and very short-lived." Exhibit C at 3. In fact, the authors of Christian used almost identical language, stating that "inflammatory responses to [flu vaccine] are mild [and] transient." Exhibit 32 at 1. As Dr. Whitton stated when evaluating the article, exhibit 32 supports the conclusion that ". . . certainly for killed influenza vaccine, [the cytokine response is] not very much and not very long." Tr. 575.

While figure 2 supports Dr. Whitton's position, figure 2 seems to contradict Dr. Levine's assertion (adopting Dr. Axelrod's argument), that the flu vaccine can induce cytokine release syndrome. Tr. 213. To repeat, she had testified that Christian supports a finding that "cytokine responses may not return to baseline in patients who have CFS." Tr. 428. First, the Christian article did not study patients who have CFS. While a study of pregnant and non-pregnant women might be the basis for drawing conclusions about people with CFS, Dr. Levine supplied no reason for this extension. Second, Dr. Levine did not justify characterizing the non-pregnant women's increase in IL-6 from approximately 0.1 pg/mL to approximately 0.2 pg/mL as "abnormal" or otherwise capable of causing injury. Third, and most importantly, the IL-6 levels did return to baseline after two days.

Exhibit 33 (Yasuyo Kashiwagi et al., Production Of Inflammatory Cytokines in Response to Diphtheria-Pertussis-Tetanus (DPT), Haemophilus Influenzae Type B (Hib), and 7-Valent Pneumococcal (PCV7) Vaccines, 10 Human Vaccines & Immunotherapies 677 (2014)) was another in vitro study examining the effect of different vaccines on levels of various cytokines. This study, however, did not examine influenza vaccine, but instead looked at DPT, HiB, and PCV7 vaccines. It appears that the main purpose of this study was to examine the effect of administering these three vaccines in combination as opposed to separately. See exhibit 33 (Kashiwagi) at 3 ("In this report, cytokine profiling was investigated using PBMCs to evaluate cytokine production in response to the stimulation of DPT, Hib, and PCV7, separately and concurrent different combinations.") Given this, the importance of the article to the present question is not entirely clear.

For his part, Dr. Axelrod states that the article stands for the proposition that "vaccination results in elevated levels of Interleukin- Iβ, Interleukin-6, Tumor Necrosis Factor-α and G-CSF. They showed that these cytokines were produced at 6 hours following vaccination and the levels increased until 24 hours." Exhibit 16 at 2. Further, he states that "[t]hey found that these elevated levels persisted." Id.

In her testimony, Dr. Levine did not explain the significance of exhibit 33. When she discussed exhibit 33, she seems to have become distracted. She said:

> Dr. Levine: In Exhibit 33, looking at a host of other sequelae of other vaccine inoculations, DPT, diphtheria tetanus, haemophilus influenza, and 7-valent pneumococcal vaccines, once again, showing on page 2 -- the kind of mechanism of how vaccine antigens – now this is on the second column, kind of the sixth line down, on page 2, 'vaccine

> antigens initiate innate immune responses by recognition of peripheral' -- I'm sorry, I'm trying to find out what the acronym PAMP stands for.
>
> DR. MIKOVITS: Pathogen associated molecular patterns.
>
> THE WITNESS: Right. At the injection site.
>
> . . .
>
> THE WITNESS: Right, right, sorry. Okay. So, the antigen, meaning the influenza virus itself, what typically happens during the immune response is that we have cells called macrophages which are just sitting in tissues and they act to present the immune -- the kind of dress-up or in some ways digest the antigen to make it presentable to the next line of defense, which are the Th1 cells that then go on to produce all kind of – it's my -- the antigen-presenting cells are migrating to the draining lymph nodes and the type 1 interferon inflammatory cytokines enhance the expression of other co-stimulatory molecules. So, once again, it's kind of on a complex process that's self-perpetuating, but then it calms down afterwards, and once again it seems that in patients with ME/CFS, that this process is -- remains ongoing.

Tr. 428-29.

Respondent's expert, Dr. Whitton, responded to the Kashiwagi article both in his expert reports and in his testimony. In his expert reports, he stated that Dr. Axelrod had misrepresented the significance of the article because nothing in the article provided evidence against his recurring statement that "in vivo cytokine production in response to these vaccines is both limited and very short-lived." Exhibit C at 3. In Dr. Whitton's testimony, he went even further, stating:

> It does not tell you the response to the cytokines produced by vaccination. What Dr. Axelrod wrote was, "Kashiwagi, et al., showed that vaccination results in elevated levels of interleukin-1b, interleukin-6, tumor necrosis factor alpha and GCSF, showed these cytokines were produced at six hours following vaccination, and the levels increased until 24 hours." That is nonsense. It's just nonsense. It's wrong.

Tr. 570.

The undersigned finds Dr. Whitton's interpretation to be more compelling than Dr. Axelrod's. As an in vitro study looking at cytokine production over a limited time course, nothing in the results counteracts respondent's position that any cytokine response to flu vaccine is "limited and very short lived."[25] For his part, respondent has never challenged that such a limited response exists. The authors of the Kashiwagi article also endorse that the results themselves do not speak to one's systemic reaction to a vaccine, noting: "[s]ince the vaccine antigen does not appear directly in blood, an experiment in which PBMCs were stimulated with vaccine antigen did not necessarily reflect the in vivo responses following vaccination." Exhibit 33 (Kashiwagi) at 683.

From the undersigned's vantage point, it does not appear that Dr. Levine adopts Dr. Axelrod's opinion that the Kashiwagi article stands for the proposition that influenza vaccination causes cytokine dysregulation. In explicating on the significance of the article, even Dr. Levine comments that following the administration of the flu vaccine antigen, the cytokine production "calms down afterwards." Tr. 429. However, she continues, by saying that the process "remains ongoing" in patients with ME/CFS. Id. It would seem, then, that Dr. Levine and Dr. Whitton are in agreement about the interpretation of the significance of Kashiwagi et al.

The rub is what happens to this limited and short-lived response in CFS patients. Dr. Levine states that in patients with CFS this process is not limited, but "remains ongoing." Tr. 429. That may be. But, exhibit 33 (Kashiwagi), which does not examine cytokine responses beyond 48 hours and does not examine the cytokine responses of individuals with CFS, does not stand for that proposition.

Exhibit 50 (Isabelle Magalhaes et al., Difference In Immune Response In Vaccinated And Unvaccinated Swedish Individuals After The 2009 Influenza Pandemic, 14 BMC Infectious Diseases 319 (2014)) was identified by Ms. Mikovits as an article that links the flu vaccine with immune dysregulation. Tr. 213. However, the relevance of exhibit 50 is unclear. Although it is one of only two articles that Ms. Mikovits explicitly cited during the hearing to support the

[25] Other special masters have drawn similar conclusions when interpreting this article. See Dean on behalf of I.D. v. Sec'y of Health & Human Servs., No. 13-808V, 2017 WL 2926605, at *17 (Fed. Cl. June 9, 2017).

claim that the flu vaccine can cause immune dysregulation, it is otherwise not commented on in this proceeding. The article, though appearing in the list of references in Ms. Mikovits' first report (exhibit 40), was not actually cited in the contents of her report. The article also does not appear in petitioner's pre-hearing brief and it was not otherwise discussed at the hearing. The only explication on the article is a note that Ms. Mikovits provided in the bibliography of her first report commenting on the significance of the article. It states: "Silent flu infections appeared to be frequent in 2009/2010. The pandemic flu vaccine induced qualitatively and quantitatively different humoral and cellular immune responses as compared to infection with the 2009 H1N1 pandemic H1N1 influenza strain." Exhibit 40 at 10. The undersigned has read the article and is uncertain about its relevance.

Exhibit 62 (Carruthers) is the article publishing the International Consensus Criteria for CFS. Dr. Levine draws attention to a section on "immune impairments." Tr. 424. Specifically, she cites the comment in the article that "A wide range of infectious agents have been reported in the subsets of patients, including [XMRV, murine leukemia virus-related viruses, enterovirus, Epstein-Barr virus, human herpes virus, chlamydia, cytomegalovirus, parvovirus, and Coxiella burnetti]." Id. (quoting exhibit 62 (Carruthers) at 332). Caruthers further notes that chronic enterovirus infection and D-lactic acid-producing bacteria have been investigated. Exhibit 62 (Carruthers) at 332.

Dr. Levine further states that: "I am suggesting and I think this is an accurate statement, that influenza vaccine in certain select individuals may act similar to these other viral agents in terms of, for instance, causing [immune dysregulation]. She concludes "so that's sort of one example in the literature which connects these infectious agents with the cytokine production." Tr. 425. Based on the respondent's reports, he appears to have never disputed that infections can cause cytokine production. In fact, his experts have explicitly said so. See exhibit H at 6-7 (noting that persistent infections from certain types of viruses have been postulated to stimulate the immune system continuously and to drive inflammation). However, respondent's experts have consistently pointed out that making an inference about the effects of a flu vaccine based on the effects of other infectious agents is fallacious for the simple fact that the flu vaccine is not equivalent to a wild infectious agent. See exhibit H at 4-6 (explicating on why the flu vaccine is not equivalent to the flu virus); exhibit F at 3 (noting how the fact that the flu vaccine is non-replicating distinguishes it from a viral infection).

Exhibit 65 (Lambert), a review article, comments on the immune response to seasonable influenza vaccination in older adults. Dr. Levine draws attention to page 3, which comments on vaccine efficacy in older adults such as Ms. McCabe. Tr. 425. The authors note that studies have found that certain antibodies are "considerably lower in vaccinated older adults than in younger adults." Exhibit 65 (Lambert) at 3. The authors refer to this as a "diminished immune response." Id. Dr. Levine also focuses on page 5, which points out that in addition to diminished immune responses, there exists a "subclinical hyperinflammatory state" in some older adults. Tr. 425; exhibit 65 (Lambert) at 5. This is due to immune cells from older adults producing higher levels of inflammatory cytokines after stimulation, which could cause constant inflammation and leave the host susceptible to disease. Exhibit 65 (Lambert) at 5. The authors speculate that this may be contributing to vaccine failure in the older population. Dr. Levine states that vaccination with an influenza virus could constitute such a "stimulation." Tr. 426. While the article is an interesting examination of how immune dysregulation could occur in older adults and how this dysregulation may cause constant inflammation, illness, and vaccine failure, it does not state how a vaccine can itself cause dysregulation. The respondent did not comment on the significance of this article.

Exhibit 66 (Jason) is a review article that presents the kindling theory of the etiology of CFS. Dr. Levine appeared somewhat confused about the significance of the article to the present question, stating that "This is the Lenny Jason paper that talks about the kindling, but there's some references to immune response as well, like page 5, in that second full paragraph." Tr. 430. The paragraph she references makes no reference to vaccinations. See exhibit 66 (Jason) at 5. The respondent's experts did not comment on the significance of this article as it pertains to the question of the influenza vaccine causing immune dysregulation.

Exhibit 68 (Devanur and Kerr) is a review article on chronic fatigue syndrome. Specifically, the article notes those viral infections that have been associated with CFS, including enteroviruses, Epstein-Barr virus, cytomegalovirus, parvovirus, hepatitis C, chlamydia, and Coxiella burnetii. Exhibit 68 (Devanur and Kerr) at 5 (table 1). Dr. Levine directs us to the statement that "It is likely that virus infection plays a role in a majority of cases of CFS." Tr. 432 (quoting exhibit 68 (Devanur and Kerr) at 5). Dr. Levine, however, states that "I don't think vaccines frequently cause these types of – your know, cause the onset, but I think they have a similar mechanism in common." Tr. 434. As noted above, the respondent does not challenge that there is an association between some infections and CFS. Nonetheless, without support, Dr. Levine seems to continue to equate

the response of the body to certain infections with the response of the body to the flu vaccine.

Exhibit 83 (Lombardi), which Ms. Mikovits co-authored, examined the chemokine profile of cases of CFS associated with XMRV. The Lombardi group of researchers discussed the work of other researchers in their review of the literature. Dr. Levine, in her testimony, highlighted two quotes from the article, each reviewing findings from other papers. In particular, Dr. Levine referenced the statement that "Natelson et al. showed elevated levels of IL-8 and IL-10 in the cerebral spinal fluid of patients with sudden, influenza-like onset CFS compared to healthy controls." Tr. 435 (referencing exhibit 83 (Lombardi) at 308). Dr. Levine also referenced the Lombardi group's statement that "Chao et al. have show (sic) neopterin and IL-6 to be up-regulated in subsets of CFS patients, indicative of a pro-inflammatory immune condition." Id. The respondent did not address exhibit 83 specifically, though, it's not clear what needs to be addressed since the exhibit does not speak about the effect of flu vaccines on immune dysregulation.

Not a single one article links the flu vaccine to immune system dysregulation. Repeatedly, as they did in their expert reports, Ms. Mikovits and Dr. Levine make leaps of logic wherein they ignore that a flu vaccine is not biologically equivalent to the influenza virus or another infectious agent. The limited articles that actually do examine the effect of the flu vaccine on the immune system merely show, consistent with the respondent's experts' opinions, mild and transient upregulation of some molecules that then return to baseline within approximately 24-48 hours. See exhibit 32. The findings from these studies appear to be entirely consistent with respondent's argument that acknowledges that vaccinations affect cytokine levels, but that the effect is "transient" and "short-lived." In other words, regulated. It is also supported by empirical evidence, as presented in respondent's exhibits M5 (Valensi), M6 (McDonald), and M7 (Eriksson). For these reasons, Ms. McCabe has failed to establish the persuasiveness of a theory that links flu vaccination to immune system dysregulation.

b. Kindling Theory

Ms. McCabe also argues that the mechanism of Ms. McCabe's disease can be explained by the "kindling" theory of CFS.[26] This theory, which was put forth

[26] Previous cases in the vaccine program have evaluated the kindling theory as it pertains to seizures, though not CFS. E.g., Adams v. Sec'y of Health & Human Servs., 76 Fed. Cl. 23, 40

by Dr. Levine, proposes a mechanism by which the flu vaccination(s) resulted in multiple low-intensity stimulations of parts of Ms. McCabe's brain, resulting in long-term neurological dysfunction that caused her CFS.

Ms. McCabe's experts are not required to support their theories with medical literature. However, expert opinion testimony without reliable support is not particularly persuasive. See Caves v. Sec'y of Health & Human Servs., 100 Fed. Cl. 119, 134 (2011) ("it should be obvious to petitioner that a scientific theory that lacks any empirical support will have limited persuasive force"), aff'd, 463 F. App'x 932 (Fed. Cir. 2012).

Here, Dr. Levine provides support for the kindling theory by citing a single article, the article that appears to be the genesis of the theory, exhibit 66 (Jason). Jason et al. speculate that the neurological phenomenon of kindling "might represent a heuristic model for understanding the etiology of [CFS]." Exhibit 66 (Jason) at 1. Referencing studies on the cause of seizures, they note that "induced seizures may increase the likelihood that more seizures will occur, since repeated stimulation lowers the threshold for more seizures to occur spontaneously after repetitive subthreshold stimuli." Id. Specifically, studies show that "if rats have their brains electrically or chemically stimulated over a period of weeks at a very low intensity that is known to be subthreshold for eliciting seizure activity, many of the rats will eventually experience epileptic convulsions." Id.

To extend these findings to CFS, Jason et al. argue that: (a) viruses activate macrophages, (b) macrophages release cytokines, (c) cytokines may alter the electrical activity of the brain. See id. at 1-2. Thus, Jason et al. propose that it may be the case that "chronically repeated low-intensity stimulation due to an infectious illness might cause kindling of the limbic-hypothalamic-pituitary axis among patients with ME/CFS." Id. at 2. According to the authors, this neurological kindling may then lead to long-term brain dysfunction that manifests as CFS. Id. Jason et al. propose the model as a way of explaining reports that CFS sometimes begins following exposure to a viral infection. Id. at 1. In other words, prior viral infections are priming patients' brains to experience the sudden onset of seizures, or seizure-like activity, and that this neuronal dysregulation causes the symptoms attributed to CFS. Id. at 1-2.

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n. 27 (2007) (noting that kindling as a model for how humans develop epilepsy is debatable in that it has only been demonstrated in a mouse).

Though exhibit 66 (Jason) is not an empirical article, it is still published under the guise of it being a peer-reviewed article that, because of peer-review, has the imprimatur of scientific soundness. While peer-review (or the lack thereof) does not establish (or preclude) reliability, meaningful peer-review is a lynchpin for the deference given to scientific publications. See Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 593 (1993); see also Terran v. Sec'y of Health & Human Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999) (stating that a special master may consider whether a theory has general acceptance in a relevant field).

There may have been a time where a judicial fact-finder could see that an article was published in a journal, such as in "Neuroscience and Medicine," and conclude that it was subject to meaningful peer-review prior to publication and thus deserves deference. However, to the extent it may have once been true, it no longer is. As the distinguished professors David H. Kaye, David E. Bernstein, and Jennifer L. Mnookin have noted, "the rise of bona fide 'open access' journals has brought with it an explosion of new titles from 'predatory publishers' purporting to have meaningful peer review and editing but willing to accept and promptly release any article that comes with a payment for the privilege." The New Wigmore: Expert Evidence § 7.6.3 (2d ed. 2018). This unfortunate reality has caused judicial officers to have to sort between legitimate journals and those that engage in the type of pay-to-play scheme referenced above. See Frater v. Hemispherx Biopharma, Inc., 996 F. Supp. 2d 335, 346 (E.D. Pa. 2014) (criticizing a party's claim that an open-source journal was "peer-reviewed" when its "self-publish, fee-based, high-acceptance model is a substantial departure from the models used by other peer-reviewed journals").

It appears that the publisher that operates the journal Neuroscience and Medicine, Scientific Research Publishing (SCIRP), is the type of predatory publisher referenced above. As reviewed by Jeffrey Beall,[27] SCIRP's practices are not consistent with a legitimate scientific publisher. Court exhibit 1001 (Five Scholarly Open Access Publishers, Charleston Advisor (2012)). After reviewing SCIRP's practices of obfuscating where it operates its business (in China, not Irvine, CA), publishing articles that have previously been published elsewhere, listing scholars as members of its editorial boards without their knowledge or permission, using spam emails to solicit article submissions, he concludes

[27] Jeffrey Beall is a research librarian who has maintained a list of predatory publishers. His list is used by, among others, some universities for the purpose of determining whether a faculty member's publication should be credited towards decisions regarding promotion and/or tenure. See Kouassi v. W. Illinois Univ., 2015 WL 2406947, at *10 (C.D. Ill. May 19, 2015).

"Scientific Research Publishing is among the sneakiest and most clever predatory Open Access publishers I have seen." Id. at 10. As for SCIRP's motivations, Mr. Beall claims that: "it exists to exploit the author-pays Open Access model to generate revenue." Id. at 9.

Jeffrey Beall's allegation of lack of meaningful peer-review in journals published by SCIRP was given substantial weight in an experiment, published in the journal Science, wherein the authors submitted "a credible but mundane scientific paper, one with such grave errors that a competent peer reviewer should easily identify it as flawed and unpublishable" to a long list of open-access journals. Court exhibit 1002 (John Bohannon, Who's Afraid of Peer Review?, 342 Science 60 (2013)). Perhaps not surprisingly, the Open Journal of Radiology, a journal published by SCIRP, accepted the article. "We are pleased to extend to you both our congratulations on the acceptance of your manuscript . . . by our journal Open Journal of Radiology (OJRad) and our heartfelt appreciation for your intellectual contribution." Id. at Supplementary Data. The authors were then advised that their article would be published after the authors paid their article processing fee. The fee for publication is currently $599. See Neuroscience and Medicine Home Page, http://www.scirp.org/journal/nm/ (last visited Apr. 17, 2018). In consideration of what is known about SCIRP's practices as a journal, it appears that giving exhibit 66 (Jason), the deference given to other peer-reviewed articles would be a mistake.

The kindling theory's lack of reputability is further confirmed by the observation that the theory, much less than being generally accepted, is not even on the radar of those who specialize in the field of immunology. Though exhibit 66 (Jason) was published in 2011, the 2015 IOM report on CFS, which dedicated a substantial portion of its 305 pages to the etiology of the disease, does not once mention the kindling theory. See exhibit M1 (IOM). Consistent with this, Dr. Leist, respondent's expert who is also the Chief of the Division of Clinical Neuroimmunology at his University, had never even heard of it. Tr. 514. The same was true for Dr. Whitton, a professor of immunology at Scripps. Tr. 619. Their unfamiliarity does not prove that the theory is not reputable, but it does support that conclusion.

In conclusion, the kindling theory does not appear to have obtained general acceptance. While the lack of general acceptance does not preclude compensation under this medical theory, it does weigh against petitioner's use of this theory to support the first prong of the Althen analysis. See Terran, 195 F.3d at 1316 (indicating that pursuant to Daubert, 509 U.S. at 592-95, a special master does not

err in considering whether a petitioner's proposed theory "enjoys general acceptance within a relevant scientific community").

Beyond the theory's lack of general acceptance, Dr. Levine's kindling theory is unpersuasive. This is for three primary reasons. The first two are intrinsic to exhibit 66 (Jason). The third is the result of how Dr. Levine applies exhibit 66 (Jason) to this case.

Addressing exhibit 66 (Jason) first, its authors do not provide meaningful support for their claim that a viral infection can induce the same type of neural stimulation as is caused by stimulatory electrodes inserted into mouse brains or by seizures. To recap, Jason et al. propose the model as a way of explaining reports that CFS sometimes begins following exposure to a viral infection. See exhibit 66 (Jason) at 1. Based on evidence that repeated subthreshold stimulation of neurons can lead to spontaneous seizure activity in those same neurons, the authors suppose that this is the mechanistic explanation for the symptoms experienced by CFS patients. Id. at 1-2. In other words, the authors are arguing that prior viral infections are priming patients' brains to experience the sudden onset of seizures, or seizure-like activity in regions of their brain. Id. However, this argument relies on the largely unsupported premise that a viral infection can cause neural stimulation that is meaningfully equivalent to the type of neuronal stimulation caused by stimulatory electrodes (as in the mouse studies that formed the basis for the empirical support for the kindling theory) or by seizures (as in the human studies showing that an initial seizure may lower the threshold for subsequent seizures).

The authors of exhibit 66 (Jason) also fail to provide meaningful support for their premise that neuronal dysregulation of the type induced by kindling is the cause of CFS. Jason et al. mention a number of ways that kindling and CFS may be linked. These include: (1) "unstable cortical excitability," (2) "high levels of oxidative stress," (3) "overstimulation of the mind or body without the available energy to act out the mental or physiological excited state," (4) "increase[d] levels of [corticotropin-releasing hormone]," (5) "sympathetic nervous system hyperactivity," (6) "[activated] serotonin and dopamine systems," (7) "increases in transforming growth factor-β," (8) "abnormally folded proteins," (9) "continuous sympathetic stimulation that would eventually lead to mental and physical exhaustion as well as glandular depletion," (10) "altered cerebral oxygenation and blood volume in the brain," and (11) "[dysregulated] mast cells and the release of histamine in the thalamus, resulting in disrupted sleep patterns." Id. at 2-8. And, of course, answer choice (12), none of the above. The sheer abundance of possible

explanations proves the point: the kindling theory of CFS is nothing more than an unsubstantiated guess. To have eleven possible explanations is to have none.

Beyond deficiencies with the contents of exhibit 66 (Jason) itself, the kindling theory, as it applies to this case, fails for a third, and even more important, reason. Adopting the theory perpetuates the unsubstantiated premise that is littered throughout petitioner's case: that receiving the flu vaccine is somehow approximate to having the flu or another infectious illness. The kindling theory proposes a link between "an infectious illness or high-intensity stimulation" which, the authors argue, repeatedly (or chronically) "kindles" activity in parts of the brain. See exhibit 66 (Jason) at 1-2. In this way, Jason et al.'s kindling theory is an attempt to explain what has already been observed: that there may be a link between certain infections and CFS. That much respondent and petitioner agree upon. However, as the respondent's experts continue to point out, the flu vaccine does not result in an immune response that approaches the effect of a wild flu virus infection. There does not appear to be evidence to support the claim that the flu vaccine results in even subclinical stimulation of the brain. Without this evidence, adopting the kindling theory is merely begging the original question.

In sum, petitioner's theories come up short of the threshold dictated by the Federal Circuit. To be sure, petitioner's burden was not to prove to a level of scientific certainty that the flu vaccine can cause CFS, but only to present a medical theory that is sufficiently reliable to allow for a meaningful examination of their claim of causation. In this case, petitioner's medical theory falls short of the lesser standard.

2. Althen Prong Three: Temporal Relationship between the Vaccination and the Injury.

Determining whether a proximate temporal relationship exists between the vaccination and the injury logically requires two different steps. First, petitioners must establish a timeframe for which it is medically acceptable to infer causation under their medical theory. Second, petitioners must show that the onset of the injury was consistent with the expected timeframe. See Shapiro v. Sec'y of Health & Human Servs., 101 Fed. Cl. 532, 542-43 (2011) (adopting this two part analysis), recons. denied after remand on other grounds, 105 Fed. Cl. 353 (2012), aff'd without op., 503 F. App'x 952 (Fed. Cir. 2013).

a. Part One: Appropriate Temporal Relationship

The initial expert reports provided little to no commentary on whether the timing of Ms. McCabe's symptoms was appropriate under the theories proffered by petitioner's experts. Ms. McCabe's was ordered to submit additional reports that addressed the appropriate timing between the vaccination and the onset of Ms. McCabe's symptoms. See order, issued Apr. 20, 2017. In response to the undersigned's prodding, Ms. McCabe filed a second report from Dr. Levine, which stated the following:

> Three days after receipt of influenza vaccine on 9/11/10 she developed full blown ME/CFS with symptoms of confusion and significant cognitive dysfunction which completely interfered with her life. The timing of the onset of her symptoms after vaccinations in this case is completely appropriate.

Exhibit 80 at 2. This statement was too conclusory to evaluate.

In the months before the hearing, the undersigned warned petitioner that her experts still had not provided a meaningful opinion on timing. See order, issued Aug. 1, 2017. Ms. McCabe subsequently filed an additional report from both Ms. Mikovits and Dr. Levine. Ms. Mikovits said:

> In summary, whether or not the prior influenza vaccines did or did not contribute to C.M.'s medical status at the time she received the September 11, 2010 vaccination, there is no question that she had been previously sensitized to the components of influenza vaccines and that the timing of her reaction to the September 11 vaccination was completely appropriate.

Exhibit 81 at 4. Dr. Levine provided the following:

> I have considered Special Master Moran's request for further clarification of the appropriate range of onset time of ME/CFS symptoms following the last flu vaccination.
>
> As stated in the record several times, Ms. McCabe received influenza vaccine on at least three occasions: October 2, 2006; October 9, 2008 and September 11, 2010. Following the first two of these influenza vaccines, Ms. McCabe complained of worsening insomnia, a key symptom of ME/CFS, 3 months later. She was more-or-less able to control her insomnia with a combination of Effexor and zolpidem. Once again, following receipt of influenza vaccine on 10/9/08, she

> was found to have 'gastritis' 2 months later, noted on endoscopy. The onset of these symptoms after these influenza vaccines is appropriate.

Exhibit 90 at 1. In the same report she added: "The temporal association completely supports the kindling theory proposed in my original report." Exhibit 90 at 2. In short, even after being directed to explain their opinion regarding timing, the experts simply stated that the timing was "completely appropriate," "appropriate," and "completely support[ive]."

At hearing, Ms. Mikovits was not any more forthcoming. Her testimony on timing is captured in this exchange with Ms. McCabe's attorney:

> Q. And was the timing of her reaction after the vaccination appropriate in this case, do you think?
>
> A. Yes.

Tr. 211.

Petitioners do not satisfy Althen's temporal relationship prong as refined and clarified in Shapiro by simply having an expert declare that the timing was "appropriate" or "completely appropriate." If saying these words were all that is required, then third prong of Althen would be rendered meaningless.

Ms. McCabe's failure to provide suitable evidence regarding the appropriate temporal relationship is explicable. As Dr. Matloubian states, petitioner's failure to develop a viable medical theory precluded a timing analysis from the outset.

> [W]ithout knowing the biologic processes that lead to development of a disease, it is impossible to define the appropriate medical time-frame that an event such as vaccination could allegedly lead to development or aggravation of that disease. This likely explains why, despite multiple opportunities to do so, Dr. Levine has been unwilling, or unable, to state what the accepted general timeframe is for vaccine-induced ME/CFS.

Exhibit L at 4.

For these reasons, Ms. McCabe has not met her burden of presenting persuasive evidence regarding the anticipated temporal relationship between vaccination and the onset of CFS.

b. Part Two: Onset of Injury

Under Shapiro's refinement of Althen's temporal relationship prong, special masters are required to determine whether the onset of the vaccinee's illness occurred within the appropriate temporal relationship. 101 Fed. Cl. at 542-43. Here, this evaluation is fanciful in that Ms. McCabe has failed to establish that she has chronic fatigue syndrome (see Section IV.A, above) and Ms. McCabe has failed to establish that her health worsened in a meaningful way after the September 11, 2010 vaccination (see Section IV.B, above). These two findings necessarily mean that Ms. McCabe cannot establish that her CFS arose (or worsened) in a temporal relationship to the flu vaccine.

Nevertheless, some additional comments regarding the alleged onset of Ms. McCabe's chronic fatigue syndrome are warranted. In Dr. Levine's final report, she stated that for the October 2, 2006 flu vaccination, "Ms. McCabe complained of worsening insomnia, a key symptom of ME/CFS, 3 months later." Exhibit 90 at 2. On its face, Dr. Levine's statement is accurate to the extent that Ms. McCabe complained of insomnia three months later. See exhibit 1 at 1. But, to the extent that Dr. Levine is implying that Ms. McCabe's January 6, 2007 complaint about insomnia was her first, this implication is wrong, if not purposefully misleading. Ms. McCabe complained of fatigue and insomnia on October 2, 2006, the date of the vaccination and the date of the first medical record in evidence. Exhibit 1 at 2. Dr. Levine does not account for this complaint. Thus, Dr. Levine has not established that Ms. McCabe's complaint reflected a "worsening insomnia" as opposed to an insomnia that is continuing.

For the October 9, 2008 flu vaccination, Dr. Levine links it to an occasion when Ms. McCabe had "gastritis." Exhibit 90 at 1. However, as Dr. Matloubian pointed out, the treating doctor diagnosed Ms. McCabe with "gastropathy," not "gastritis." Exhibit L at 1. Dr. Levine has not persuasively explained why "gastropathy" is a precursor to chronic fatigue syndrome.

Finally, with respect to the critical vaccine—the September 11, 2010 flu vaccine, Dr. Levine opined that three days later, Ms. McCabe "developed full blown ME/CFS with symptoms of confusion and significant cognitive dysfunction which completely interfered with her life." Exhibit 80 at 2. The source for Dr. Levine's statement that problems started three days later is not entirely clear as Ms. McCabe told doctors at NYU Hospital on September

22, 2010, that she had problems the day she received the flu vaccination but went to work two days later. Exhibit 2 at 6. Furthermore, the assertion that Ms. McCabe's "significant cognitive dysfunction . . . completely interfered with her life" is contradicted by the reports of neurologists who found Ms. McCabe neurologically and cognitively normal. Dr. Levine's assertion is also inconsistent with the Wankel Hardware store earnings report, which shows that Ms. McCabe continued to work there in the quarter after the vaccination.

Consequently, even if the other substantial problems with Ms. McCabe's were set aside and only the opinions regarding timing were evaluated, Ms. McCabe's proof on prong three would still fall short.

3. Althen Prong Two: Logical Sequence of Cause and Effect Showing that the Vaccination was the Reason for Ms. McCabe's putative C.F.S.

Evidence of a viable medical theory and temporal proximity between the vaccine and the injury is strong evidence of causation. However, the Federal Circuit has also said that this evidence is not enough. Althen, 418 F.3d at 1278 ("[a]lthough probative, neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation"). In Capizzano, the Federal Circuit further expounded upon the importance of evaluating whether a logical sequence of cause and effect exists independently of the timing analysis. Specifically, the Capizzano panel stated "There may well be a circumstance where it is found that a vaccine can cause the injury at issue and where the injury was temporally proximate to the vaccination, but it is illogical to conclude that the injury was actually caused by the vaccine." 440 F.3d at 1327. Thus, special masters must consider the whole picture and determine, on the basis of all the evidence, if the purported connection between the vaccine and the injury is logical. Examples of some of the evidence that special masters may consider here include the opinions of treating physicians and medical experts, evidence of rechallenge, epidemiological studies, and the probability of coincidence or another cause. See id. The evidence available to be weighed will, of course, depend on the facts of the case.

In this case, there does not appear to be an injury nor does there appear to be evidence presented demonstrating the appropriate temporal proximity between the putative injury and the vaccination. Thus, the analysis here serves little purpose for the ultimate question of causation since concluding causation appears to, by

now, be precluded. However, given the facts of this case, the analysis remains important for how it exemplifies how almost every piece of evidence in this case weighs against Ms. McCabe's petition for compensation.

The Federal Circuit has emphasized that the opinions of treating physicians are important. Id. at 1326 ("treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury"). No treating physician, despite the many that have evaluated Ms. McCabe, has diagnosed her with CFS, much less associated that CFS with the flu vaccination. Furthermore, no treating physician has associated any present symptom of Ms. McCabe's, regardless of the diagnosis, with her flu vaccination. The fact that no treating physician has associated the vaccine to her symptoms is especially conspicuous since Ms. McCabe has proclaimed to almost all of them that the flu vaccine was the cause of her ongoing symptoms. The unwillingness for a single physician that treated Ms. McCabe to, even tentatively, associate the two speaks loudly.

In addition, there exists a quite salient alternate cause to the symptoms Ms. McCabe experienced following her September 11, 2010 flu vaccine. As noted above, Ms. McCabe's overall condition, in terms of her fatigue, depression, and insomnia does not appear to have appreciably changed following the flu vaccine. She appears to present with the same set of symptoms at approximately the same frequency. However, Ms. McCabe did report that she felt especially ill following the September 11, 2010 flu vaccine and that she ultimately ended up going to the NYU emergency room because of these symptoms. This visit appears to mark the only part of Ms. McCabe's medical history that stands out as being notable in relation to the rest of her medical records. When she appeared at the emergency room, the physician evaluated her and concluded that she most likely had a viral illness. Exhibit 2 at 9. The respondent's experts agree with this diagnosis and conclude it also explains Ms. McCabe's symptoms following the flu vaccine. Tr. 682. Petitioner's medical expert has never counteracted this diagnosis. The undersigned sees no reason, nor has been given any reason, to undermine the physicians' diagnosis.

V. Conclusion

The evidence does not support that Ms. McCabe has the disorder she claims she has. In fact, the evidence does not support that she had a change in health following the flu vaccine at all. For those reasons alone, Ms. McCabe's petition for compensation must fail.

However, to avoid any inference that the rest of Ms. McCabe's case was strong, if not colorable, her claim of causation-in-fact was also evaluated. Ms. McCabe did not present a plausible theory for how a flu vaccine can cause the injury she alleges she has and she cannot explain how the facts in her case are consistent with this theory. In short, nothing in petitioner's case supports a finding of causation. Thus, Ms. McCabe's petition is DENIED.

The Clerk's Office is instructed to enter judgment in accord with this decision.

IT IS SO ORDERED.

s/ Christian J. Moran
Christian J. Moran
Special Master